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SATURDAY APRIL 1 1950

TABLE OF CONTENTS

Sarcoidosis, with Special Reference to Lung Changes J. G. SCADDING, M.D., F.R.C.P. ..745

Amyloidosis in Rheumatoid Arthritis G. H. JENNINGS, M.D., F.R.C.P. ..753

Medical Administration in the Tropics GEORGE MACLEAN, C.B.E., M.B. ..756

Trial of Procaine Penicillin Preparations E. GRIFFITHS, F.R.C.S., A. J. WALKER, F.R.C.S., and R. A. SHOOTER, M.D. ..761

Cancer of the Uterus in Adrenogenitalism HUGH C. MCLAREN, M.D., F.R.C.S.Ed. ..763

Erysipeloid of Rosenbach MARTIN A. GOODWIN, M.B., F.R.C.S.Ed. ..765

Coracoclavicular Joint F. J. S. HALL, O.B.E., M.B., F.R.C.S.Ed. ..766

MEDICAL MEMORANDA

Recovery from Ruptured Mycotic Aneurysm. PHILIP R. GRAVES, M.D., M.R.C.P., and I. J. BRODIE RUSSELL, M.B., Ch.B. ..768

Skin Eruption in Newborn due to Bromism Derived from Mother's Milk. GEO. T. C. YEUNG, M.B., B.S. ..769

REFRESHER COURSE

Headache. J. PURDON MARTIN, M.D., F.R.C.P. ..778

GENERAL ARTICLES AND NEWS

The Scientific Method ..781
New Medical Bill ..782
Iodine and Goitre ..783
New Clamp for Portocaval Anastomosis. FRANCIS E. STOCK, F.R.C.S. ..784
MEDICAL NOTES IN PARLIAMENT ..792
UNIVERSITIES AND COLLEGES ..794
MEDICAL NEWS ..795
BIRTHS, MARRIAGES, AND DEATHS ..796

REVIEWS

Pathology of Neurosurgery ..770
Common Fevers ..770
A Thyroid Revolution? ..770
Medical Protozoology ..771
Books Received ..771

MEDICO-LEGAL

Damages for Blood Donor ..792

Epidemiology Section ..794

LEADING ARTICLES

Infectious Mononucleosis ..772
Assistants in General Practice ..773
Sarcoidosis ..774
Health Administration in the Colonies ..775

ANNOTATIONS

New Medical Bill ..776
Macrocytic Anaemia in Liver Disease ..776
Procaine Penicillin Preparations ..777

OBITUARY

F. W. Twort, M.R.C.S., F.R.S. ..788
A. H. Proctor, D.S.O., M.D., M.S., F.R.C.S.Ed. ..789
S. Vere Pearson, M.D., M.R.C.P. ..790
A. H. Evans, O.B.E., M.D., M.S., F.R.C.S. 791
T. H. Milroy, D.Sc., M.D., F.R.S.Ed. ..791
G. T. K. Maurice, C.M.G., C.B.E., M.R.C.S. 791
Robley H. J. Browne, O.B.E., M.R.C.S. ..791

SUPPLEMENT

General Practitioners' Remuneration—Health Service Estimates—Bill for First Nine Months—Special Inducement Fund—Whitley Council—Senior Hospital Medical Officers—Dental Service for Children—Registration of Opticians ..109
REGISTRARS GROUP ..110
HEARD AT HEADQUARTERS ..111
MEDICAL ETHICS ..111
CORRESPONDENCE ..111
B.M.A. FILM LIBRARY ..114
ASSOCIATION NOTICES ..114

CORRESPONDENCE

Intrathoracic Goitre. T. HOLMES SELLORS, M.Ch., F.R.C.S. ..784
Maternity and the N.H.S. R. L. RIDGE, M.B.; JAMES ROSS, M.B.; W. YOUNG, M.B.; J. E. KENNEDY, L.R.C.P. ..784
An Appendicular Faecolith. CHARLES WELLS, F.R.C.S. ..785
Acute Laryngo-tracheo-bronchitis. IVOR H. C. BALFOUR, M.D., and PETER C. RUSHTON, M.R.C.S.; FRANK FALKNER, M.R.C.S. ..786
Speech Disorders in Childhood. A. A. E. NEWTH, M.B. ..786
Adrenal Cortical Tumours. R. R. WILSON, M.D. ..787
Anaesthesia for Fenestration Operation. C. LANGTON HEWER, M.R.C.P.; D. R. RIGG, M.B., and R. P. PARKER, M.B. ..787
Sadism on the Screen. CLIFFORD ALLEN, M.D. ..787
A Useful Hobby. ROBERT CRAWFORD, M.B. ..788

QUESTIONS AND COMMENTS

Viability of Common Bacteria—Acute Dilatation of the Stomach in Poliomyelitis—Ejaculatio Praecox—Residual Insecticides—Preparation for Dental Extractions—Dicoumarol in Thrombophlebitis—Toxic Effects of Vitamin D — Urticaria Pigmentosa — Delayed-action Hypnotic—Holidays Abroad—Amphetamine and Benedict's Solution—Teething Troubles—Jelly-fish and Weever-fish ..797–8

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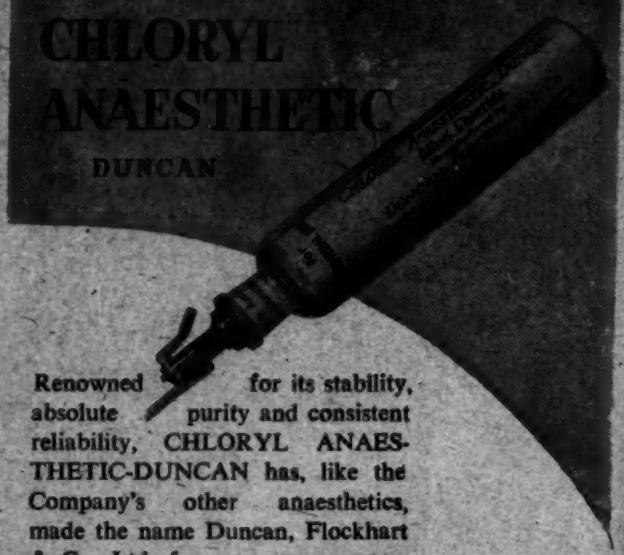

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 1 1950

SARCOIDOSIS, WITH SPECIAL REFERENCE TO LUNG CHANGES*

BY

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[WITH PHOTOGRAVURE PLATE]

The syndrome to which the name sarcoidosis has come to be generally applied in the Anglo-American literature may seem at first to be of rather rare occurrence and too specialized to form the subject of this lecture. Yet there are few subjects whose study leads into more varied fields of investigation. The more frequent manifestations of the syndrome have led to clinical interest in it by dermatologists, by ophthalmologists, and by physicians concerned with diseases of the respiratory system; while occasional manifestations have aroused the interest also of neurologists and endocrinologists. A study of its peculiar immunological aspects involves a study of the vast field of the immunology of tuberculosis; the study of its pathology and morbid histology cannot be dissociated from studies of similar aspects of tuberculosis, of the reticuloses, of tissue reactions to other infections such as brucellosis, and of foreign-body reactions; and the similarity of the clinical and pathological changes induced by exposure to certain beryllium salts to those of sarcoidosis leads into the field of industrial disease. Thus no subject could better illustrate the essential unity of medicine.

Clear definition of terms is essential to clear thought. Medical literature contains many examples of the fallacy which springs from neglect of this principle: the fallacy introduced by failure to start with a clear definition of terms, and consequent failure to perceive that the same term has been used with different meanings in different parts of the argument. For instance, in the controversy about the relation of sarcoidosis to tuberculosis it is not uncommon to find that the argument has been started as if in the definition the question of the relation to tuberculosis had been left open; while, in collecting the data, cases which show all features of the syndrome but in which tubercle bacilli happened to have been found have been excluded. The failure to start with clear definition also leads to a number of circular arguments in the various controversies about the disease. For instance, many physicians include in their concept of sarcoidosis, whether specifically formulated or not, the idea that in this syndrome tuberculin sensitivity must be either absent or slight. To such physicians questions about the tuberculin test in sarcoidosis will clearly be not factual but purely verbal; the answer to them will require no examination of data but simply elucidation and examination of definitions. This is a fallacy into which physicians studying the pulmonary and other systemic manifestations of the syndrome have fallen, rather than the dermatologists. The latter can use the equivalent of an ostensive definition, involving no proviso stated or implied about the tuberculin test; they simply say that by the various forms of sarcoid of the skin they mean lesions like others which they have observed, and which they describe either in words or, better, by illustration or demonstration. Thus the statements of dermatologists about the proportion of their cases showing a positive tuberculin reaction are more likely to have factual content than the statements of chest physicians.

Definition of Sarcoidosis

Having said this I must admit that clear definition of the syndrome is very difficult. It is significant that very many papers and reviews on this subject start with a fairly extensive historical survey mentioning the contributions of Hutchinson (1877), Besnier (1889), Boeck (1899, 1905), Schaumann (1914, 1936), Jüngling (1919), and others to our concept of the syndrome. This procedure avoids the difficulty of formal definition; it answers the question, "What disease are you talking about?" by saying, "The disease that has been described in these classical papers." It leaves as the sole criterion of whether a given case should be classified in the group under discussion its similarity to the classical descriptions. It leaves open the question which part of the classical descriptions should be regarded as essential and which incidental, and has made way for much unfortunate wrangling about priority of description and for a confusing variety of eponyms. As well as the eponyms, several other names have been used; among these I favour "sarcoidosis," because, although the word could be reduced to nonsense by strict etymological examination, it could also be interpreted rather more freely as denoting that group of cases in which there are generalized changes having a similar histology to that of the skin lesions which the dermatologists have named sarcoids. It also has the advantage of being free from aetiological implications.

In general it has been agreed that the most important common distinguishing feature of the group is a histological pattern, consisting of epithelioid cell tubercles, as a rule clearly defined within the affected tissue, with only slight round-cell infiltration in their vicinity, without central caseation, with or without Langhans-type giant cells, and with or without the peculiar inclusion bodies within these cells described by Schaumann (1941), proceeding in the older lesions to conversion into a peculiar hyaline type of fibrous connective tissue. The striking uniformity of these appearances in the most characteristic cases has

*The Bradshaw Lecture delivered at the Royal College of Physicians of London on November 10, 1949.

suggested to some the possibility of correlation of the histological changes with a specific aetiology.

This appearance, however, cannot be regarded as specific to any one aetiological agent. Although typical sarcoid lesions are easily distinguishable from those of classical tuberculosis, individual lesions can be found in cases of classical tuberculosis which resemble in every respect sarcoid tubercles. In erythema nodosum, presumably of tuberculous origin, van Beek and Haex (1948) state that tubercles, some having all the characteristics of sarcoid tubercles, can be found in a high proportion of cases in liver tissue obtained by aspiration biopsy. In chronic brucellosis, lesions have been found in the liver and in the bone marrow, both by biopsy and at necropsy, which very closely resemble sarcoid tubercles, though from the published reports (Spink and Sundberg, 1947; Spink *et al.*, 1949) it seems to me that there is more round-cell infiltration in and around the lesions, and the lesions are less clearly circumscribed in the tissue, than is present in typical sarcoids; and the granulomatous lesions following chronic exposure to beryllium may resemble the non-caseating tubercle of sarcoidosis very closely (Hardy and Tabershaw, 1946; Dutra, 1948; Grier *et al.*, 1948; Pascucci, 1948; Martland *et al.*, 1948). Hence, although a histological appearance must be described as an essential part of the definition of sarcoidosis, it does not provide the criterion of an aetiologically distinct group. Yet any other criteria that may be added are likely to be permissive and thus blur rather than sharpen the definition. Let us consider the definition of sarcoidosis by the conference on sarcoid of the U.S. National Research Council (quoted by Ricker and Clark, 1949).

"Sarcoidosis is a disease of unknown aetiology. Pathologically it is characterized by the presence in any organ or tissue of epithelioid cell tubercles with inconspicuous or no necrosis and by the frequent presence of refractile or apparently calcified bodies in the giant cells of the tubercles. The characteristic lesions may be replaced by fibrosis, hyalinization, or both. Clinically, the lesions may be widely disseminated. The tissues most frequently involved are lymph nodes, lungs, skin, eyes, and bones, particularly of the extremities. The clinical course usually is chronic with minimal or no constitutional symptoms; however, there may be acute phases, characterized by a general reaction with malaise and fever. There may be signs and symptoms referable to the tissues and organs involved. The intracutaneous tuberculin test is frequently negative; the plasma globulins are often increased. The outcome may be clinical recovery with radiographic evidence of residue, or impairment of function of organs involved, or a continued chronic course of the disease."

The many permissive phrases at the end of this definition ("there may be acute phases" . . . "the tuberculin test is frequently negative; the plasma globulins are often increased. The outcome may be clinical recovery") leave the door wide open to difference of clinical opinion about which cases should be classified under the heading "sarcoidosis." Moreover, the definition as it stands would include cases of chronic beryllium granulomatosis, since these satisfy all its criteria—unless these cases be taken to be excluded by the preliminary statement that sarcoidosis is a disease of unknown aetiology. However, this phrase carries its own difficulties with it, especially for those who believe that sarcoidosis, at least in some cases, is a manifestation of tuberculosis; since, as soon as in any given case they have succeeded in proving their contention, this interpretation of the definition logically excludes the case from the category of sarcoidosis. I consider that the only way out of these dilemmas is to adhere strictly to a careful histological definition. It will be necessary to add to the description of the characteristic histological appearances the proviso that they must be present in all affected tissues; the finding of a few isolated lesions presenting these characteristics accompanying more extensive lesions with different characteristics should not be allowed to bring the case as a whole in the category of sarcoidosis. This proviso would exclude the occasional sarcoid-like lesion in a case of classical tuberculosis and the sarcoid-like lesions which have been found to occur in certain situations in chronic brucellosis. Adopting this definition, it will be perfectly proper logically to speak of tuberculous sarcoidosis, of beryllium sarcoidosis, of sarcoidosis due to any other agent that may possibly in future be shown to cause it, and of sarcoidosis of undetermined cause. We can then hope that the number of cases relegated to the latter group will steadily diminish as our knowledge of the condition and our methods of investigating it advance.

Incidence of Pulmonary Sarcoidosis

My purpose is to review, mainly from a clinical point of view, the pulmonary disorders associated with this disease process. The frequency of cases in which the lungs are involved in sarcoidosis in the general population is difficult to estimate, since the only figures likely to be available are those from mass radiography, and the diagnosis by this means is only presumptive. Schönholzer (1947) stated that in 67 out of 516,879 mass radiographic examinations in the Swiss Army appearances suggesting a diagnosis of pulmonary sarcoidosis were found, an incidence of 0.13 per 1,000.

The incidence of sarcoidosis varies with race. In all large series from the United States there is evidence of a higher incidence in the negro section of the population of that country. Ricker and Clark (1949), who examined the records of the United States Army Institute of Pathology, found that 174 of 300 cases were in negroes; since negroes constituted 10% of the United States Army, they estimated that the disease must have been about 17 times as frequent in the negroes as in the whites. Similarly McCort *et al.* (1947) found that, of 28 patients referred to a United States Army centre for radiotherapy on account of lymphadenopathy who were found to be suffering from sarcoidosis, 15 were negroes. Twenty-three of Longcope's (1941) 31 patients were negroes. Harrell (1940) found that of 11 cases in North Carolina 9 were in negroes. Fourteen of the 36 cases reported by Garland (1947) in California were in negroes. Thirty of the 35 cases which Reisner (1944) observed in New York were in negroes.

In a series of cases diagnosed clinically as sarcoidosis the incidence of involvement of individual organs varies, as would be expected, according to the source of the cases. A high proportion of cases coming under the care of dermatologists on account of skin lesions show intrathoracic changes. Kissmeyer (1932) found that of 24 cases of skin sarcoidosis 19 showed intrathoracic changes on radioscopy. Vosbein and Bonnevie (1940) found intrathoracic changes in 10 out of 16 cases showing typical skin lesions. Nielsen (1934) found lung changes in 37 out of 39 cases of cutaneous sarcoidosis. Reisner (1944) found that 33 out of 35 cases coming under observation in chest clinics showed lung lesions, and 30 enlarged intrathoracic lymph nodes. McCort *et al.* (1947) reported 28 cases seen in an Army Hospital centre for radiotherapy, and therefore coming under observation primarily because of enlarged hilar or peripheral lymph nodes; 15 of these had radiological evidence of lung involvement. Ricker

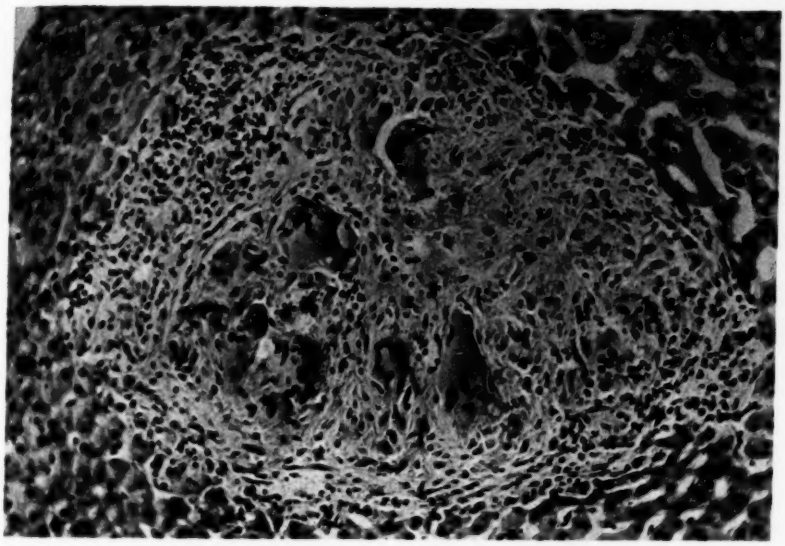

FIG. 1.—Case 4. Liver biopsy. (× 160.)

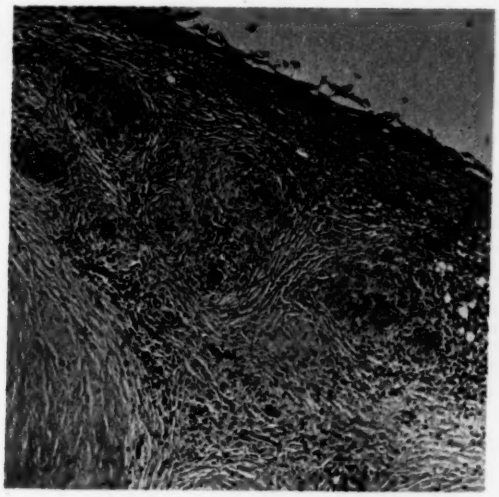

FIG. 2.—Case 16. Biopsy of supraclavicular lymph node. (× 55.)

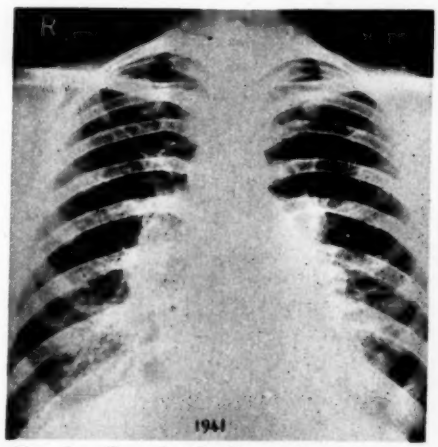

FIG. 3.—Case 6. Radiograph of chest in 1941.

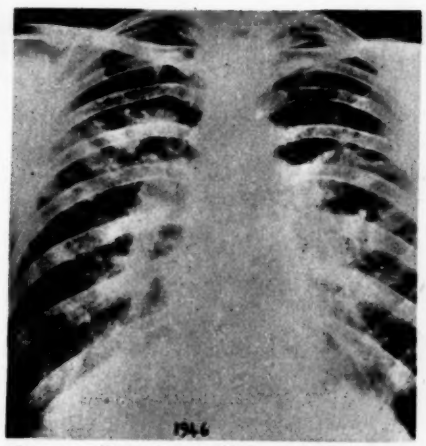

FIG. 4.—Case 6. Radiograph of chest in 1946.

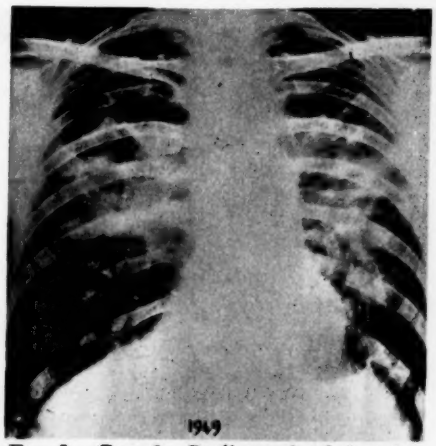

FIG. 5.—Case 6. Radiograph of chest in 1949.

FIG. 6.—Case 10. Radiograph of chest, showing part of right lung.

FIG. 7.—Case 10. The same one month after four months' calciferol treatment.

J. G. SCADDING: SARCOIDOSIS, WITH SPECIAL REFERENCE TO LUNG CHANGES

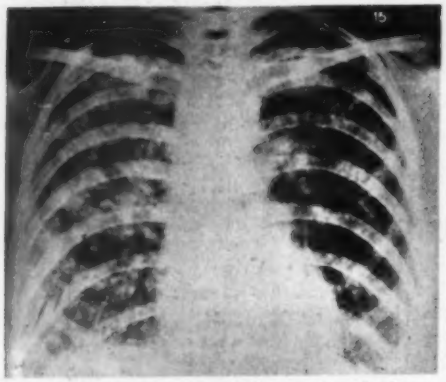

FIG. 8.—Case 11. Radiograph of chest: January, 1948.

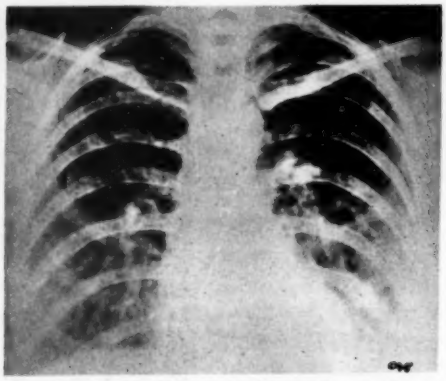

FIG. 9.—Case 11. Radiograph of chest; April, 1949.

FIG. 10.—Case 16. Radiograph of chest: June, 1949.

FIG. 11.—Case 16. Radiograph of chest; August, 1949.

H. C. McLAREN: CANCER OF UTERUS IN ADRENOGENITALISM

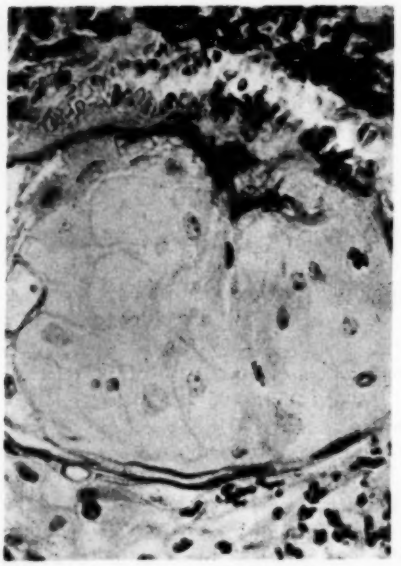

FIG. 1.—Adeno-acanthoma with circumscribed pale area. (× 480.)

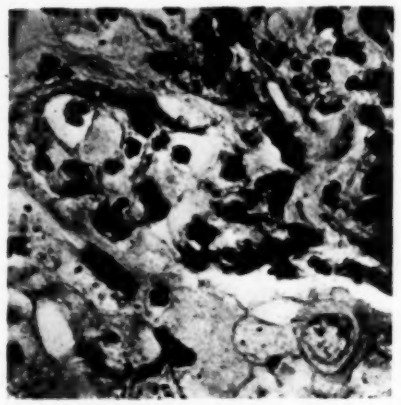

FIG. 2.—Metaplasia. Cytoplasm of irregularly shaped epithelial cells is pale staining with hæmatoxylin-eosin; some of the nuclei are fragmented. (× 480.)

G. H. JENNINGS: AMYLOIDOSIS IN RHEUMATOID ARTHRITIS

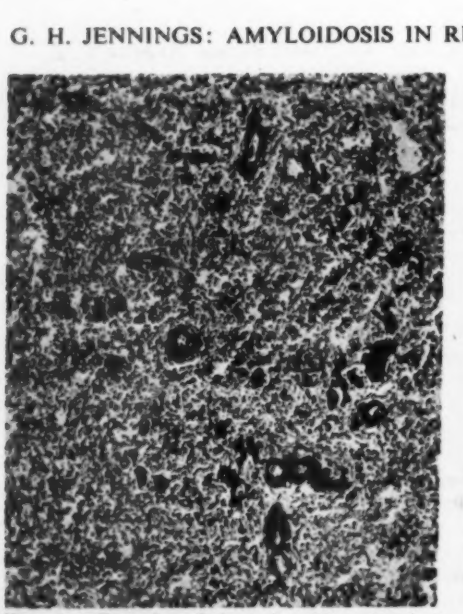

FIG. 1.—Case 2. Spleen (× 85). Methyl violet stain shows amyloid in central arteriole of Malpighian corpuscle and in smaller arteriolar branches around periphery.

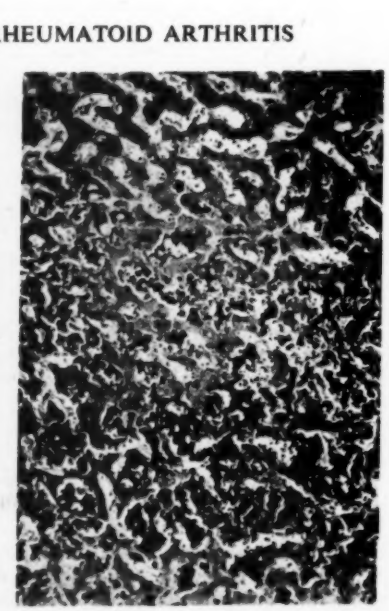

FIG. 2.—Case 2. Liver (× 85). Dark-staining amyloid material between sinus endothelium and compressed, degenerated liver cells.

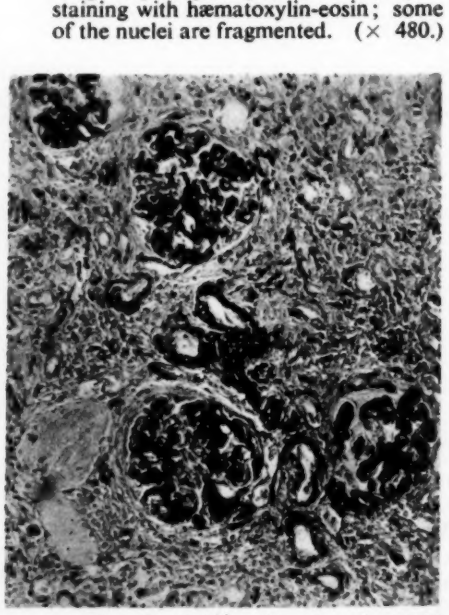

FIG. 3.—Case 2. Kidney (× 85). Amyloid changes in glomeruli and afferent arterioles; tubular degeneration; replacement fibrosis.

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and Clark (1949) found evidence of involvement of the lungs in 36% of 300 cases from which pathological material, either biopsy or necropsy, had been examined at the United States Army Institute of Pathology. Of the 13 cases reported by Snapper from a general medical clinic in 1938, 9 showed lung lesions. In my own 16 cases the lungs were involved in 15 and there was gross enlargement of hilar glands in the other; this finding is of course largely a reflection of my interest in diseases of the chest.

Types of Change in the Chest Radiograph in Sarcoidosis

In the 12 years since I first became interested in this syndrome, interrupted by the war years, I have observed 16 cases in which I made a diagnosis of sarcoidosis. In 13 of these the diagnosis was supported by histological evidence; in the remaining three no suitable tissue was obtained for histological examination, and the diagnosis therefore remained one of clinical probability. I propose to describe briefly the changes in the chest radiographs in these cases; and in an attempt to elucidate the natural history of the lung changes I will classify the cases into groups according to the changes evident in the first available radiograph. In several instances this was made several years before I first saw the patient. In the following description, enlargement of hilar lymph nodes indicates enlargement sufficient to be evident in a plain postero-anterior radiograph. In all cases examination of sputa or other material (e.g., stomach contents) for tubercle bacilli, usually including culture or guinea-pig inoculation, has been performed and yielded negative results, except where otherwise stated.

1. Enlargement of Hilar Lymph Nodes Without Detectable Lung Change

Three cases presented enlargement of the hilar lymph nodes without detectable lung change in the first available chest radiograph; the enlargement was unilateral in one and bilateral in two.

Case 1 (Case 2 of Scadding and Sherlock, 1948).—A man aged 24 had had recurrent bilateral chronic iridocyclitis for 18 months. The spleen was enlarged. The Mantoux test was positive to 0.1 mg. old tuberculin. There were no superficial lymph nodes available for biopsy, but liver biopsy showed typical non-caseating tubercles without giant cells. The first chest radiograph showed enlargement of the right hilar lymph nodes. After treatment with calciferol the ocular condition became quiescent and the lymph nodes subsided in about a year.

Case 2.—A woman aged 35 had been treated in 1937 for an apical tuberculous lesion, though no bacilli had been found. In 1939 she developed grossly enlarged bilateral hilar lymph nodes without symptoms. The only abnormality found on physical examination was slight enlargement of lymph nodes above the inner ends of both clavicles, biopsy of one of which showed characteristic non-caseating tubercles. The Mantoux reaction was persistently negative to 10 mg. O.T. After about a year a diffuse infiltration developed in both lungs, again without symptoms, and both it and the enlarged lymph nodes disappeared gradually over the course of the next two or three years. In 1946, shortly after the birth of a healthy child, the Mantoux reaction was found to be positive to 0.1 mg. O.T. Seen recently, she remained well, and the chest radiograph showed only the old apical scar.

Case 3.—In 1931 a woman then aged 24 developed skin lesions first on the legs and then on the arms (Fig. A). Biopsy of the skin showed characteristic sarcoid lesions. Soon after the appearance of the skin lesions she developed chronic iridocyclitis. This subsided in about two years. In 1936 she complained of cough, substernal discomfort, dyspnoea, and loss of weight, and was found to have enlarged hilar lymph nodes. She was treated in a sanatorium. Pulmonary infiltration developed while she was there. When I saw her in 1938 the hilar nodes had diminished considerably in size, but there was diffuse mottling, densest in the middle zones, of a quality suggesting some fibrosis. The skin lesions were still present. The subsequent course of this patient has been briefly reported by Hoyle (1947). Tubercle bacilli appeared in the sputum shortly before death from right heart failure in 1946.

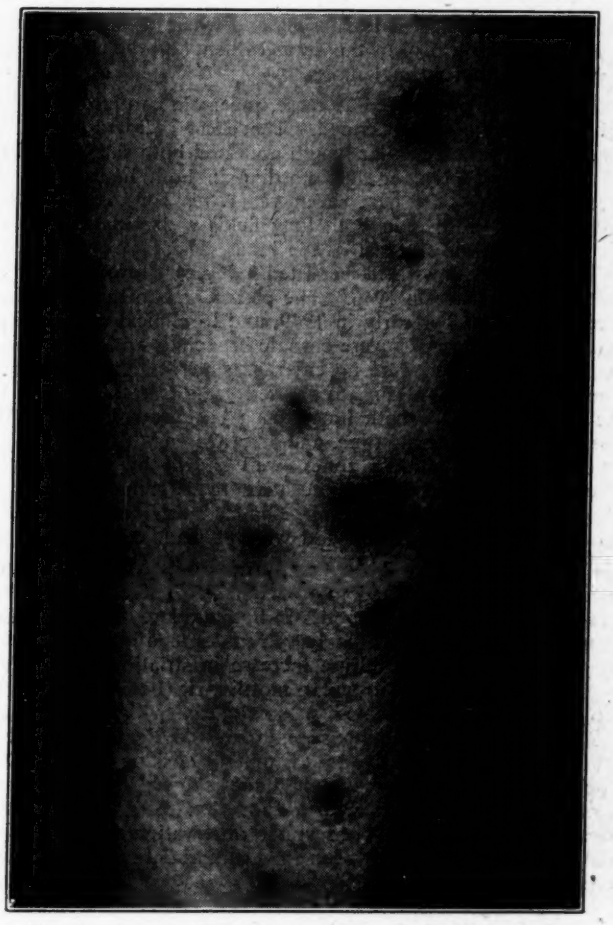

FIG. A.—Case 3. Skin lesions on leg. Similar lesions were present on arms and forearms.

2. Bilateral Enlarged Lymph Nodes With Diffuse Mottling in the Lungs

In four cases the first available chest radiograph showed gross bilateral hilar-lymph-node enlargement with diffuse infiltrations in the lungs of various sorts.

Case 4.—A man aged 32 complained of pain in the left side of the chest for about five weeks followed by some dyspnoea and loss of over a stone (6.35 kg.) in weight. A radiograph showed bilateral hilar-lymph-node enlargement with some faint fine mottling in the lower zones of the lungs. There were no enlarged superficial lymph nodes. The Mantoux test was positive to 0.1 mg. O.T. Liver biopsy showed one small non-caseating epithelioid-cell tubercle with giant cells (Plate, Fig. 1). The symptoms disappeared within three months, and the chest radiograph became normal within nine months without any special treatment.

Case 5.—A man aged 27 was referred to hospital in 1943 on account of progressive enlargement of the cervical lymph nodes for 14 months, followed by swelling of the inguinal lymph nodes. On physical examination generalized enlargement of lymph nodes in all superficial groups was found. The Mantoux test (dose not recorded) was reported negative. Biopsy of a cervical node showed characteristic epithelioid-cell tubercles with some giant cells but not caseation. A chest radiograph showed some enlargement of hilar lymph nodes together with a diffuse mottling in the lung fields. Shortly after this the

superficial nodes started to subside, and when he was next seen in 1949 no enlargement of them was evident and the chest radiograph was within normal limits.

Case 6.—A woman aged 28 came under observation first with a history of two years' cough. The chest radiograph at this time showed enlarged hilar lymph nodes on both sides, together with an irregular rather fine mottling in both lungs (Fig. 3). In the course of the next seven years this condition steadily progressed to fibrosis in both lung fields with gross emphysematous changes in the rest of the lungs, where, however, some miliary-type shadows still persisted. Fig. 4 shows the radiographic appearance in 1946. The patient was in this condition when I first saw her early in 1949, and to clinical examination presented a picture of severe chronic bronchitis with spasm and emphysema. There were no enlarged superficial lymph nodes. The chest radiograph (Fig. 5) showed gross fibrotic changes in the middle zones of both lungs, on a background of the old-standing diffuse fine mottling, and emphysema with large bullae especially in the middle zones, well shown by tomography. The Mantoux reaction was negative to 10 mg. O.T. Liver biopsy showed several small non-caseating epithelioid-cell tubercles without caseation and without giant cells.

Case 7.—A woman aged 38 complained of two years' lassitude, breathlessness, cough, and loss of weight. There were moderately enlarged soft lymph nodes in both axillae. A chest radiograph showed enlarged hilar lymph nodes (confirmed by tomography), together with diffuse increase in striations throughout both lungs and some irregular mottling in both lower zones. Tomography also revealed a small cavity-like appearance, probably an emphysematous bulla, at the right apex. The Mantoux test was negative to 0.1 mg. but positive to 1 mg. O.T. Biopsy of an axillary lymph node showed many discrete epithelioid-cell tubercles with a few giant cells and no caseation. The patient has been under observation for only eight months and there has been no substantial change in her condition.

3. Diffuse Pulmonary Infiltration Without Gross Evidence of Hilar-Lymph-Node Enlargement

In the first available chest radiograph seven cases showed diffuse pulmonary infiltrations without gross enlargement of the hilar lymph nodes. The infiltrations varied from a fine approximately miliary type to an irregular coarser type, and were in some cases followed by irregular fibrotic changes.

Case 8.—A man aged 19 was found on radiography, undertaken because when he was medically examined for the Army he complained of two months' dry cough, to have a diffuse fine mottling throughout both lung fields. On examination there were no abnormal physical signs. The Mantoux test was positive to 0.01 mg. O.T. There were no superficial lymph nodes for biopsy, and liver biopsy showed no abnormality. In this case a diagnosis of sarcoidosis was made by exclusion. His condition has remained unchanged in one year's observation.

Case 9.—A man aged 19 complained of cough, slight dyspnoea, and some loss of weight. On physical examination the spleen was just palpable and there were a few not very notably enlarged lymph nodes palpable in both axillae. A radiograph of the chest showed diffuse fine rather reticular mottling. The Mantoux reaction was negative to 10 mg. O.T. Biopsy of an axillary lymph node showed no specific changes, and an attempt at liver biopsy was unsuccessful in obtaining tissue. The diagnosis of sarcoidosis was made on clinical grounds. After four months' treatment with calciferol, 150,000 units a day, there was a slight though appreciable diminution in the density of the shadows.

Case 10.—A woman aged 23 complained of four months' cough, pain in the chest, and dyspnoea. There were no abnormal physical signs. A chest radiograph showed a diffuse rather coarse pseudo-miliary infiltration in both lungs (Fig. 6). The Mantoux test was positive to 0.01 mg. O.T. Liver biopsy showed no specific changes. She was treated for four months with calciferol, which was followed by striking resolution of the abnormal shadows (Fig. 7).

Case 11 (Case 1 of Scadding and Sherlock, 1948).—A woman aged 22 was found by mass radiography in November, 1945, to have a coarse diffuse bilateral infiltration of both lungs. She was symptom-free. On physical examination the only abnormality was enlargement of lymph nodes behind the inner ends of both clavicles and in both epitrochlear regions. The Mantoux test was negative to 10 mg. O.T. Biopsy of one of the cervical lymph nodes and of the liver showed typical non-caseating tubercles. Under observation the infiltration became gradually denser, and during 1947 she steadily lost weight and the sedimentation rate rose. At the end of this year new lesions were found in some of the phalanges of the hands and feet. At this stage (Fig. 8) she was treated with calciferol in dosage varying from 50,000 to 100,000 units daily, adjusted according to her tolerance, for five months. This was followed by very striking clearing of the abnormal shadows (Fig. 9) and by a great increase in weight with reversion of the sedimentation rate to a normal level.

Case 12.—A man aged 35 was found on routine radiography to have diffuse irregular mottling in both lungs maximal in the middle zones. Physical examination revealed some soft enlargement of lymph nodes in the left axilla and the liver edge was palpable. The Mantoux test was negative to 10 mg. O.T. Biopsy of an axillary lymph node showed non-caseating epithelioid-cell tubercles with giant cells. After four months' treatment with calciferol, 150,000 units a day, which was well tolerated, there was some diminution in the density of the abnormal shadows in the lungs.

Case 13.—A man aged 31 complained of increasing dyspnoea for five years and cough for six months. On physical examination the only abnormality was slight enlargement of lymph nodes above the left clavicle, in both axillae, and in the groins. A chest radiograph showed widespread coarse mottling throughout both lungs. The Mantoux test was negative to 1 mg. but positive to 10 mg. O.T. Biopsy of a lymph node showed non-caseating epithelioid-cell tubercles with many giant cells. He proved intolerant of calciferol. Six days' administration of 50,000 units daily produced severe toxic symptoms.

Case 14.—A man aged 35 complained of increasing dyspnoea and cough with scanty sputum. Shortly before the first radiograph in 1946 he had had an acute illness with pain in the right side of the chest. This radiograph showed diffuse fine mottling through both lung fields with a more homogeneous shadow indicative of consolidation in the right middle lobe. A year later, in September, 1947, the density of the pulmonary infiltration had increased. In July, 1948, enlargement of lymph nodes on both sides of the neck was noted, and a biopsy showed many epithelioid-cell tubercles without caseation. In November, 1948, when I first saw him, he was noticeably dyspnoeic on slight exertion; there were enlarged lymph nodes in both sides of the neck, in the axillae, and in the groins. In June, 1949, when he was admitted for investigation, the radiographic appearances remained similar to those seen in the previous November. Tomography showed evidence of cavitation or emphysematous bulla formation in both middle zones. The Mantoux test was negative to 10 mg. O.T. Biopsy of a lymph node showed many discrete epithelioid-cell tubercles, with some areas of hyaline fibrosis. He proved intolerant of calciferol. Recently, without any immediate change in his symptoms, tubercle bacilli were found in his sputum for the first time, confirmed by culture; and the Mantoux test has become positive.

4. Fine Reticulation

One patient whose only complaint was of dyspnoea showed a very fine reticulated appearance in the chest radiograph which might quite easily be missed on casual inspection of the film.

Case 15 (Case 3 of Scadding and Sherlock, 1948).—A woman aged 40 complained of increasing dyspnoea, especially over the past 18 months, an almost unproductive cough, some pain across the chest, and loss of weight. On physical examination there

was considerable enlargement of lymph nodes in the left axilla, the spleen was easily palpable, and there were fine scattered rales throughout both lungs. The chest radiograph showed fine diffuse reticulation maximal in the upper and middle zones. The Mantoux test was negative to 1 mg. O.T. Biopsy of a left axillary lymph node showed many epithelioid-cell tubercles with some giant cells but no caseation, and biopsy of the liver revealed a discrete lesion with a hyaline connective-tissue centre, surrounded by epithelioid cells, young fibroblasts, and some round cells, but no giant cells. In 2½ years' observation there has been little change in her condition, although in April, 1949, accompanying an intercurrent respiratory infection, she developed a transient atelectasis of the right middle lobe, which subsequently re-expanded.

5. Fibrosis, Emphysema, and Bulla Formation

One patient first came under observation in the late stage with fibrosis, emphysema, and bulla formation.

Case 16.—A woman aged 41 when first seen in June, 1949, complained that she had not felt well since the birth of her third child in 1946. In June, 1947, she had started to suffer from pain and stiffness in the small joints of the hands, wrists, elbows, shoulders, hips, and knees. Early in 1948 she had an acute illness diagnosed as pneumonia. In the summer of 1948 cough gradually developed with about ½ oz. (14 ml.) of purulent sputum. At this time the rheumatic pains ceased and have not recurred. The cough and sputum, however, gradually became worse. Early in 1949 the cough and sputum became much worse and she was admitted to a hospital for two months. At this time it was reported that acid-fast bacilli had been seen in small numbers in the sputum, but on culture shortly afterwards no tubercle bacilli were grown. When I first saw her in June, 1949, she was thin, with no clubbing of the fingers and no abnormal signs, apart from those in the chest, except for a very firm mobile lymph node behind the inner end of the right clavicle. The chest radiograph (Fig. 10) showed diffuse mottling in the left lung maximal in the middle and lower zones, and in the right lung similar mottling partly obscured by a dense opacity with a cavity and fluid level in the middle zone. The Mantoux test was negative to 1 mg. O.T. Biopsy of the supraclavicular lymph node (Fig. 2) showed a central mass of collagen with a number of small active follicles of epithelioid cells and some giant cells at the periphery. There was no evidence of caseation and no tubercle bacilli were seen on fluorescence microscopy. Inoculation of two guinea-pigs from this lymph node and repeated cultures of the sputum were all negative for tubercle bacilli. The diagnosis of sarcoidosis with either pyogenic infection in an emphysematous bulla or intercurrent abscess was made. An attempt was made to treat the abscess on the right side by postural drainage and penicillin. This unfortunately resulted in secondary abscess formation in the left lung (Fig. 11), and tomograms at the beginning of August demonstrated the cavitation in both lungs very clearly. She has been treated intensively with penicillin for the secondary infection with relatively little success, though some diminution in the pneumonic densities is evident. Recently the spleen has become palpable.

Natural History of the Lung Changes

Correlating my own experience with reports in the literature, I think the earliest intrathoracic lesion of sarcoidosis is usually hilar-lymph-node enlargement, which may be shortly followed or more rarely accompanied by a more or less diffuse pulmonary infiltration varying from a fine micro-nodular type resembling miliary tuberculosis to coarser irregular mottling. Possibly some cases start with the pulmonary infiltration without a preceding stage of hilar-lymph-node enlargement. Infiltrations of either type may either clear completely so far as radiographic appearances are concerned, or persist for a variable time with a variable amount of replacement by fibrosis. This fibrosis most frequently takes the form of irregular coarse strands, usually in the middle zones, with gross emphysematous changes elsewhere; or it may more rarely be of much finer type giving rise to a fine reticulated appearance in the radiograph. This latter appearance may easily be missed on inspection of the radiograph; it is accompanied, however, by a considerable diminution in the patient's vital capacity and correspondingly severe functional disability. In the cases which present the picture of fibrosis and emphysema tubercle bacilli may eventually appear in the sputum, although the radiographic appearances may not show any immediate corresponding change.

The question of cavitation in sarcoidosis without frank tuberculosis merits some attention. Gross and obvious cavity appearances were an important feature in Case 16, which, as stated above, presented with a picture suggesting diffuse fibrotic changes in the lungs with abscess formation. I think that this was probably due to secondary infection in emphysematous bullae. Three other cases have shown gross emphysematous bulla formation, and one case had a small very high apical cavity, detectable with certainty only by tomography.

Pulmonary cavitation without evidence of classical tuberculosis has been reported previously in sarcoidosis by several observers. Ustvedt (1948) reported the necropsy appearances in a woman aged 39 who had suffered from Heerfordt's syndrome for 11 years before death and had had respiratory symptoms for two years. At necropsy there were large cavities at both apices without characteristic histological changes, either tuberculous or sarcoid, in their walls, together with generalized fibrotic and bronchiectatic changes in the lungs. Tice and Sweany (1941) reported the case of a woman aged 45 who had shown a characteristic sequence of changes in the chest radiograph starting with enlargement of the mediastinal shadows and irregular nodular infiltration in the lungs. At necropsy a cavity with a fibrotic "capsule" was found in the right lower lobe. Emphysematous changes, often with gross bullae, have been frequent findings in post-mortem examinations (Pinner, 1938; Rubin and Pinner, 1944): Schaumann (1933) and Hogan (1946) have published clinical and necropsy reports on patients whose lungs presented radiographic appearances closely similar to those observed in cases 6 and 14 of my series. Clinical reports of patients showing radiographic appearances suggesting gross cavitation have been made by Salvesen (1935), by Pruvost and Depierre (1946), and by Bernstein and Sussman (1945).

Diagnosis

Confirmation of the diagnosis of sarcoidosis depends upon histology. It is important to recall that the definition adopted above demands that the characteristic changes should be present in all affected tissues; hence the discovery of such changes in a single biopsy specimen is not absolute proof of the diagnosis, but is evidence to be added to clinical, radiological, and other evidence. In many cases superficial lymph nodes are available for biopsy and provide the most accessible material. When lymph nodes are not available it has been shown that liver biopsy, even though there is no clinical evidence of affection of that organ, often shows characteristic lesions (van Beek and Haex, 1943a, 1943b; van Buchem, 1946; Scadding and Sherlock, 1948). If skin lesions are present these of course offer convenient biopsy material. Some Scandinavian workers have recommended biopsy of tonsils, which, even if they appear normal, often show characteristic changes in sarcoidosis; I have not had occasion to adopt this rather severe method. In my series of 16 cases tissue was obtained by lymph-node biopsy in 10, of which nine

gave positive results; by liver biopsy in seven, of which five gave positive results; and from the skin in one.

Differential Diagnosis

In the cases of my series, classical tuberculosis was the condition from which differentiation was most frequently difficult. Cases 5, 6, 7, 9, and 10 all showed at some stage an appearance which would have been compatible with a diagnosis of chronic miliary tuberculosis. They were regarded as falling into the sarcoid group because of their good general condition, in some cases because of their insensitivity to tuberculin, and because of the clinical course. It must be admitted, however, that the differentiation between chronic miliary tuberculosis and sarcoidosis is in many instances little more than a verbal one. Cases 3, 11, and 13 presented radiological appearances consistent with a diffuse tuberculous infiltration of a coarser type, and again it was consideration of all aspects which led to their being classified in the sarcoid group. Cases 3, 6, 14, and 16 all showed at some stage a picture of pulmonary fibrosis with gross emphysema and either cavity formation or emphysematous bullae. These cases at this stage closely simulated the late stage of chronic indolent fibrotic pulmonary tuberculosis; and in fact in two of them tubercle bacilli appeared eventually in the sputum, and in another in an earlier stage acid fast bacilli were once seen in the sputum, though they could not be cultured, and perhaps too much significance should not be attached to this latter finding.

Difficulty sometimes arises in the differential diagnosis of sarcoidosis from industrial lung disease of varied sorts. This difficulty arose in Case 14. This patient had been employed for many years in a cement works. However, there was no recognized incidence of industrial pulmonary disease in the works, and the typical sequence of radiographic changes together with the generalized lymphadenopathy which showed typical sarcoid changes left no doubt of the diagnosis. It is possible, of course, that the exposure to dust may have had some effect in modifying the radiographic appearances of the sarcoidosis. In the more recent cases specific inquiry was made about possible exposure to beryllium, with negative result; and it is highly improbable that this factor entered into the aetiology of the earlier cases.

My own opinion of the aetiology of the cases in my series is that they fall into the category of tuberculous sarcoidosis. In most of them this opinion is supported by collateral evidence only, and there are admittedly strong arguments which could be advanced against it; but in two cases (Nos. 3 and 14), as noted above, acid-fast bacilli appeared eventually in the sputum, and in one (Case 2) the history suggests that a patient originally suffering from classical tuberculosis went through a "sarcoid" phase. Perhaps if I had the courage of my convictions I should follow the lead of Pinner (1938), which he himself subsequently abandoned, and label my cases "non-caseating tuberculosis."

Treatment

Arsenic (Snapper and Pompen, 1938), tuberculin (Irgang, 1939), and *x*-ray therapy have been tried for the treatment of sarcoidosis, but with no general agreement about their value. Since many clinicians believe most cases of sarcoidosis to be of tuberculous origin, a trial of streptomycin might be expected to have been undertaken. However, it is well recognized that streptomycin is most effective in the acute exudative types of tuberculosis and relatively little, if at all, effective in the most productive types; and the lesions of sarcoidosis are the perfect example of the productive non-exudative reaction. Hence, *a priori*, streptomycin would not be expected to have much effect on them even if they are of tuberculous origin; and in the only reference to the use of streptomycin in sarcoidosis which I can find, Pulaski and White (1948) state that they have treated seven cases of pulmonary sarcoidosis with streptomycin without effect on the pulmonary lesions.

After the success of calciferol in the treatment of lupus vulgaris it would have been surprising if dermatologists had not tried calciferol for cutaneous sarcoids. However, I can find only very scanty reference to this in the literature. Dowling and Prosser Thomas (1946) referred to one case of sarcoid which had proved unresponsive to calciferol. Curtis, Taylor, and Grekin (1947) reported a series of five cases treated with calciferol and dihydrotachysterol with generally satisfactory results; several of their patients showed toxic reactions.

Calciferol treatment has been tried in nine of my patients At first I attempted to give the dose usually employed in lupus vulgaris—namely, 150,000 units a day. The first patient treated was Case 11. When treatment was begun she had been under observation for over two years, during the last six months of which the pulmonary infiltration had become notably denser, there had been loss of weight and a rise in the sedimentation rate, and fresh lesions had appeared in the bones of the hands. Treatment was started with 150,000 units daily, but she soon developed nausea and anorexia and showed a brisk rise of serum calcium together with a slight rise in blood urea. She was maintained on doses varying between 50,000 and 100,000 units a day, depending upon the blood chemical findings, for five months. At the end of this time there was some improvement in the lung lesions, and one month later a most dramatic clearing was evident; the lungs have remained clear apart from a little scarring in the right upper zone during the 15 months that have elapsed since then.

Of the nine cases in which calciferol treatment has been attempted, three tolerated 150,000 units daily, three tolerated only smaller dosage, and three were completely intolerant. This proportion of intolerant cases is much greater than has been reported in series composed of patients most of whom have been treated for conditions other than sarcoidosis: Anning, Dawson, Dolby, and Ingram (1948) reported that of their 200 patients treated with large doses of calciferol 19% developed toxic symptoms, but apparently not severe enough to prohibit further attempts in therapy in most. In the three completely intolerant cases in my series sensitivity to calciferol was remarkable. The accompanying chart shows briefly the response of one patient (Case 13) to a dose as small as 50,000 units daily for six days. The administration of only 10,000 units a day when the condition appeared to be improving was sufficient to cause a return of symptoms

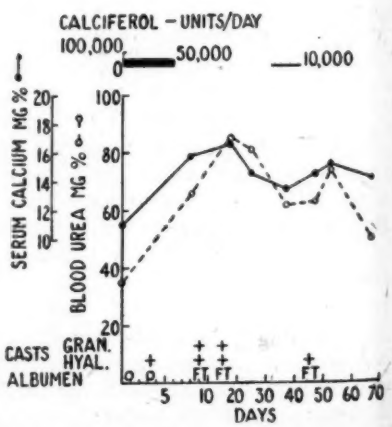

FIG. B.—Chart showing biochemical effects of administration of calciferol. 50,000 units daily, for six days in Case 13 FT = faint trace.

and a relapse in the biochemical changes. The other two patients (Cases 7 and 14) showed equally severe symptomatic and biochemical evidence of toxicity, but after larger doses of calciferol. It is unfortunate that complete investigations of the renal function were not made before treatment was started in these cases, since it is known that sarcoid lesions sometimes occur in the kidneys (Horton, Lincoln, and Pinner, 1939; Cameron and Dawson, 1946), and it is therefore possible that there may have been some preceding impairment of the renal function. The ordinary ward tests had revealed no abnormalities in the urines. In future I shall certainly investigate the renal function before treating any case of sarcoidosis with calciferol. All the six patients who tolerated calciferol showed some degree of improvement. Three tolerated 150,000 units a day for four months. Of these, one (Case 10) showed complete clearing of the lung lesions and two (Cases 9 and 12) showed some improvement. Three (including the one already quoted) tolerated smaller doses varying from 50,000 to 100,000 units daily. Of these, one case (Case 11) showed complete clearing of the lung infiltration, and one (Case 6) diminution in density of miliary type shadows, though established fibrotic and emphysematous changes remained unchanged. In the remaining patient (Case 1) calciferol was given because of persistently active bilateral iridocyclitis, and the only intrathoracic change was enlargement of the right hilar lymph nodes; the iridocyclitis became quiet and the hilar nodes subsided after the calciferol, and there has been no evidence of renewed activity under observation for two years afterwards.

The progress of the patients in whom treatment with calciferol was attempted is summarized in the accompanying Table, together with the progress of the patients not

Progress of Lung Lesions in 16 Cases of Sarcoidosis in Relation to Administration of Calciferol

	Tolerated Daily Dose Units	Progress of Lung Lesion			Worse	Death
		Cleared	Improved	Unchanged		
Treatment attempted (9 cases) ..	150,000	1	2	0	0	0
	50,000–100,000	2	1	0	0	0
	Intolerant	0	0	2	1	0
Treatment not attempted* (7 cases) ..	—	3	0	3	0	1

* This includes the cases with the longest observation periods.

so treated. No conclusion can, of course, be drawn from these data. The average period of observation of the cases in which treatment was attempted is considerably shorter than that for those untreated; and the difference between the progress of the patients intolerant of calciferol and that of those in whom treatment was possible may be explained as well by the hypothesis that patients whose lesions are in an actively progressing phase do not tolerate calciferol as by the hypothesis that calciferol benefited the patients who tolerated it. Nevertheless, I think that the effect of calciferol on the diffuse pulmonary infiltrations of sarcoidosis is well worth further investigation.

Prognosis of the Lung Lesions

Summing up the progress of the 16 cases after periods of observation varying from 8 months to 15 years: one has died in right heart failure with tubercle bacilli in the sputum; six have shown complete clearing of the radiographic abnormality, with or without calciferol treatment; two have shown increase in the extent and severity of the pathological process under observation, and in one of these tubercle bacilli have recently appeared in the sputum; and seven have shown no change, some of them after only short periods of observation. A similarly variable course of the pulmonary lesions has been reported by others. Bruce and Wassen (1940) found that of seven cases showing pulmonary lesions four cleared and three remained unchanged after periods of observation varying from one to three years. King (1941) reported a follow-up of 37 cases, in 23 of which the intrathoracic lesions had cleared or almost cleared in periods varying from seven weeks to three years, with an average of 22 months after first detection; in three there had been some clearing; in eight no change occurred after periods varying from three months to four years; and in three the lesions extended after intervals of seven months, eight months, and four years. Garland (1947) reported that in 36 cases there were two deaths; of 17 followed for periods varying from six months to seven years the lesions regressed in ten, were static in four, and progressed in three. Reisner (1944) followed 27 cases with lung changes and found that the lesion regressed in thirteen, was static in five, and progressed in nine. Six patients developed clinical tuberculosis and two died with generalized tuberculosis. Reisner thought that the disseminated nodular form especially showed a tendency to regression of the lesions. This view is consistent with the findings in my series.

Lung Changes in Tuberculin-negative Cases of Erythema Nodosum

It is now generally agreed that erythema nodosum should be regarded as a cutaneous response which may be elicited by a variety of agents. In respect of several of these, there is good evidence that the response occurs after sensitization to the agent concerned and may therefore be called allergic. This is certainly the case in the common type of erythema nodosum which appears soon after primary tuberculous infection; in these a high degree of tuberculin sensitivity is almost always found. Great interest therefore attaches to a group of cases which present a nodose erythema of typical distribution, with enlargement of hilar lymph nodes, usually bilateral, often with an extensive but transient and symptomless pulmonary infiltration, and in which tuberculin sensitivity, when tested, has been found to be absent or slight. Attention was first directed to these cases by Scandinavian workers (quoted by Forssman, 1946). In this country Kerley (1942, 1943) has recorded 37 cases which appear to belong to this group, though tuberculin tests were performed in only three of them.

Dr. Neville Oswald has recently brought to my notice a case which illustrates this group, and has kindly allowed me to quote it.

Case 17.—A nurse aged 51 noticed an eruption on the legs, later extending to the thighs, but otherwise felt well apart from some slight breathlessness, which, however, did not prevent her carrying out her full day's work. Her general condition was good and no abnormal signs were discoverable on examination apart from about 18 typical erythema nodosum lesions on the legs. The Mantoux test was negative to 1 mg. O.T. A biopsy of one of the lesions on the leg was reported to show a non-specific reaction consistent with erythema nodosum. A radiograph of the chest showed bilateral enlargement of the hilar lymph nodes, well demonstrated in a tomogram, together with a diffuse infiltration throughout both lungs; and in radiographs of the hand small well-defined rarefactions were evident in several of the phalanges.

Skiöld (1945) reviewed 354 cases of erythema nodosum and found that 35 of them had bilateral hilar-lymph-node

enlargement; none of these showed any evidence of frank tuberculosis. Of 91 cases with evidence of tuberculosis all showed unilateral hilar enlargement and none bilateral. Löfgren (1946) reviewed 178 cases of erythema nodosum and found that 102 showed unilateral and 30 bilateral hilar-lymph-node enlargement. Six of those with bilateral enlargement showed a miliary pulmonary infiltration; in two of these, histological appearances suggesting sarcoidosis were discovered—in a lymph node in one and in the skin in the other. Nine of the cases with bilateral hilar-lymph-node enlargement had negative or weak tuberculin reactions. He found the histology of the erythema nodosum the same whether the tuberculin tests were negative or positive. Bjerkelund (1947) reported the case of a woman aged 48 who had erythema nodosum with bilateral hilar-lymph-node enlargement and a Mantoux reaction negative to 1 mg. O.T. Later she developed successively a transient miliary infiltration in the lungs, areas of rarefaction in bones of the fingers, and a subcutaneous nodule which gave a typical histological appearance of sarcoidosis; the biopsy of the original erythema nodosum had shown no specific histological changes.

Thus there is strong evidence that the syndrome of Mantoux-negative erythema nodosum with bilateral hilar-lymph-node enlargement is related to sarcoidosis. Whether this group can be sharply differentiated from the group associated with frank tuberculosis remains doubtful. The difficulty of differentiation is well shown by the work of van Beek and Haex (1948), to which reference has already been made. They performed liver biopsy in 10 cases of erythema nodosum which appeared to be of frankly tuberculous type and found tubercles in seven, and in several of these the tubercles were of the type seen in sarcoidosis; their patients all had positive tuberculin skin reactions. If the hypotheses (*a*) that this particular group of Mantoux-negative erythema nodosum cases is indeed related to sarcoidosis and (*b*) that sarcoidosis is a manifestation of tuberculosis in a subject with a peculiar "anergic" reaction to the infection be accepted, it is surprising that a rash which in frankly tuberculous cases commonly occurs at a time when allergic hypersensitivity is present, and in fact is often regarded as an indication of the presence of such hypersensitivity, should also occur in a phase of the infection characterized by anergy. It is probably this discrepancy which has led some observers to adduce the Mantoux-negative erythema nodosum cases with sarcoid characteristics as evidence for an unidentified agent as the cause of sarcoidosis; Kerley (1943) even suggests that it supports the hypothesis that this agent is a fungus largely by analogy with coccidioidomycosis, in the primary stage of which erythema nodosum is frequent. For those who hold that sarcoidosis is frequently of tuberculous origin Mantoux-negative erythema nodosum with evidence of sarcoidosis presents a fascinating problem, the solution of which may help towards a more complete understanding not only of sarcoidosis and of erythema nodosum but also of immunity and allergy in tuberculosis and other infections.

Conclusion and Summary

In this lecture I have confined my attention to the clinical aspects of the pulmonary manifestations of sarcoidosis. Of the pathology, even of the lung lesions, and of beryllium sarcoidosis, I have had time to say little; manifestations in the skin, the bones, the lymph nodes, the eye, and the kidney have been mentioned only in passing, and of the nervous system, the salivary glands, the endocrine glands, the heart, and the gastro-intestinal tract not at all. I have been unable to deal with the very interesting problems of skin-sensitivity to tuberculin, of procutins and anticutins, of the Kveim reaction, and of the results of B.C.G. vaccination in cases of sarcoidosis.

A definition of sarcoidosis on a strictly histological basis has been suggested in order that it should be logically possible to refer to sarcoidosis of established aetiology—for example, to tuberculous sarcoidosis and to beryllium sarcoidosis.

The lung changes start usually with a diffuse infiltration accompanying or shortly following a bilateral hilar-lymph-node enlargement. This infiltration varies from a fine miliary type to a coarse irregular mottling. In about half the cases this infiltration clears completely. In the rest, slowly progressive fibrosis, usually in coarse strands maximal in the middle zones, replaces the infiltration, and secondary emphysema, often bullous, develops. In patients who have reached this stage tubercle bacilli may appear in the sputum, and the prognosis is then poor.

Calciferol treatment seems worth further trial in the cases with diffuse infiltrations, though many patients tolerate it poorly and it should therefore be given cautiously and with strict biochemical control.

Mantoux-negative erythema nodosum with bilateral hilar-lymph-node enlargement often shows other features suggestive of a relation to sarcoidosis, and may prove a fruitful field of study.

I am indebted to the chest physicians who, knowing my interest in this subject, have referred cases to me, and especially to Drs G. E. Fearn and H. Broderick for allowing me to use their radiographs in Cases 6 and 14, and to Dr. B. G. Edelston for a complete account of the early history of Case 16; to Dr. H. K. Meller, who referred Case 15 to me and has carried out most of the follow-up; to Dr. Clifford Hoyle, who continued the observation of Case 1 during the war years; to Dr. J. W. Crofton for allowing me to quote Case 5, which was under his care; and to Dr. Neville Oswald for Case 17. I am also indebted to Mr. E. V. Willmott for the photomicrographs, and to him and to Mr. D. F. Kemp for the photographs of the *x*-ray films.

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AMYLOIDOSIS IN RHEUMATOID ARTHRITIS

BY

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[WITH PHOTOGRAVURE PLATE]

The association of amyloid disease and rheumatoid arthritis was described first by Whitman (1903) in an account of two cases of Still's disease with enlarged liver and spleen: the one of these patients who died was proved to have gross amyloidosis in the liver, spleen, kidneys, and mesenteric glands. This patient, like all those since recorded with associated rheumatoid arthritis and amyloidosis, was emaciated. In 1906 Beattie described four cases in which patients between 19 and 28 years of age had had relapsing acute rheumatism for from seven months to four years. All four patients died, and amyloid disease was found in their liver, spleen, and kidneys. In the three in whom diarrhoea was noted amyloid changes were found in the villi of the small intestine.

No further case of rheumatoid arthritis and amyloidosis was described until 1927, when Carroll and Nelson reported a fatal example in a boy with Still's disease. Since this case fewer than 50 cases have appeared in the literature. By 1944 Trasoff *et al.* had collected 14 cases of amyloidosis in Still's disease and 17 in adult rheumatoid arthritis. In 1947 Yeoman and Wilson referred to 30 adult cases of rheumatoid arthritis with amyloidosis. To this number can be added the two following cases.

Case 1

A female warehouse assistant aged 23 had an attack of tonsillitis during the summer of 1943. This was followed by stiffness and swelling of the knees, ankles, wrists, and fingers. The swelling persisted with fluctuations up to the time of her admission to this hospital five years later. During that time, both in and out of hospital, she had received dental treatment, physiotherapy to the affected joints and neighbouring muscles, vitamin concentrates, iron, one course of auro-calcium, and two courses of sodium aurothiomalate ("myocrisin"). These courses consisted of weekly injections; the first (12 injections) totalled 0.6 g., the second (20 injections) 1 g., and the third (13 injections) 0.95 g. Urine was normal throughout.

The affected joints settled with the first two courses, but chronic deformities were marked in the hands and wrists at the end of the second course. She rested two months, and the E.S.R. was then (June 24, 1947) 38 mm. Slight exercise was allowed and improvement was maintained, though there was occasional pain in the joints, and on September 2, 1947, the E.S.R. was 24 mm. During the third course of gold injections, which then followed, she had occasional attacks of petit mal, but remained fairly well until early March, 1948, and was able to walk, which she could not do from 1945 to 1947. At the beginning of March both knees became painful, hot, and swollen, and she was again unable to walk. She also became generally ill, pale, and febrile (temperature 99.8° F. (37.7° C.), pulse 110). There was loss of weight, but no severe sweating. As the knee-joints did not settle she was admitted to Edgware General Hospital, and was kept under treatment (mostly in bed) for three months.

When admitted on May 5, 1948, she was thin, flushed but anaemic, with marked dental sepsis and gum infection. Severe bilateral chronic deformity of the hands and wrists was present, and neither elbow could be fully extended. There was moderate movement in the wrists, but finger flexion was much impaired. Both knees were swollen, warm, and painful; the left, which was more markedly affected, could not be fully extended. The liver was greatly enlarged and the spleen just palpable (Fig. A). Puncture biopsy (June 2) proved the liver enlargement to be due to amyloid.

FIG. A.—Case 1 nine months after discharge from ward. In spite of improvement she still shows gross liver and slight splenic enlargement. Rheumatoid changes in knees, wrists, and fingers are present and muscular wasting is still evident.

With physiotherapy (including splinting) and the elimination of dental sepsis the knee swellings settled considerably, and both knees could not only be fully extended but also had a fair degree of flexion. By the time of her discharge she was able to walk with help, and the E.S.R. had by then fallen from 89 to 68 mm. There was a low-grade fever (99–100° F.—37.2–37.8°C.) during the first nine weeks, but this settled gradually to normal during the last four weeks in hospital. A course of systemic penicillin (500,000 units daily) was given for three weeks, and a *Bact. coli* urinary infection was eliminated with sulphonamides. She was also given iron (ferrous sulphate 18 gr. (1.2 g.) daily) and ascorbic acid. Her haemoglobin rose from 50% to 90% (Haldane) and the red blood cells from 4,120,000 to 5,180,000 during her stay in hospital. She was discharged on August 7, 1948.

Since her discharge she has had oral whole liver as well as iron and ascorbic acid, and physiotherapy has been continued. The enlargement of the liver and spleen has persisted unchanged to the time of writing (September 10, 1949). Her knee-joints, elbows, wrists, fingers, and ankles still show chronic rheumatoid deformity (Fig. A), but only the right hip is painful. It is also very stiff, as are the fingers, but all other joints have a satisfactory range of movement, so that she can progress a little on crutches. Her general condition is slightly improved and there is no oedema. Her blood pressure was 110/80.

Investigations During Stay in Hospital.—Radiographs on May 14, 1948, revealed chronic rheumatoid arthritis of long standing in hands and wrists, with moderate osteoporosis and destruction of articular surfaces. The knees showed an early stage of rheumatoid arthritis, with no bone destruction or rarefaction, but with diminished joint spaces. The teeth showed apical rarefaction and sepsis as well as cavitation in places.

On May 5 the plasma proteins were : total, 7.5 g.% ; albumin, 3.6 g.% ; globulin, 3.9 g.% The serum alkaline phosphatase was 8.7 units (King and Armstrong). The thymol turbidity was negative. The blood W.R. was negative, and the blood-sugar curve on May 5 was within normal limits. On July 19 the urine showed : protein +++, few white blood cells, and occasional granular and hyaline casts.

Investigations Since Discharge.—The plasma proteins on December 5, 1948, were : total, 7.5 g.% ; albumin, 4.4 g.% ; globulin, 3.1 g.%. On June 24, 1949, they were : total, 8 g.% ; albumin, 3.8 g.% ; globulin, 4.2 g.%. At that date the urine showed : protein +++, white blood cells, and a few hyaline casts ; and on September 2 : protein +++ and a few granular casts. The blood urea on June 24 was 27 mg. per 100 ml. A blood count on July 1 showed : red cells, 4,800,000 per c.mm. ; Hb, 74% (Haldane) ; C.I., 0.77 ; white cells, 4,400 (normal differential). On October 11 it showed : red cells, 5,700,000 per c.mm. ; Hb, 72% (Haldane) ; C.I., 0.64 ; white cells, 4,600. The E.S.R. (Westergren) was 51 mm. in the first hour on July 1, and 6 mm. on September 2. A radiograph of the hips on June 27, 1949, revealed an eburnating arthritis, more marked on the right side. The joint spaces were much diminished, but there was no bony ankylosis and the bone was of normal density. The hands and wrists were unchanged.

Case 2

A man aged 65 was admitted to Edgware General Hospital on April 16, 1949, shortly after having a large haematemesis with melaena. Previous history was of rheumatoid arthritis for about four years which had been treated at the Red Cross Clinic, Peto Place, for three years. His knees and feet were first involved, and on March 26, 1946, a radiograph of the left knee showed slight narrowing of the joint space, with periarticular thickening. He received a course of auro-calcium between May 29 and September 5, 1946, and then, when a total of 0.11 g. had been given, a slight but persistent albuminuria caused the treatment to be stopped. Physiotherapy was continued, but he made no real improvement. On November 12 his wrists, fingers, and knees showed marked rheumatoid changes, and radiographs of these joints revealed the characteristic osteoporosis and loss of joint cartilage. His E.S.R. (Westergren) remained at about 80 mm. throughout the latter half of 1946, but by April 10, 1947, it had risen to 100 mm. Routine blood counts throughout this period showed no abnormality, but by the end of 1948 his haemoglobin level was 49% (Haldane).

On March 14, 1949, his general condition and joint condition were much worse. The knees were fixed in flexion, and the fingers, wrists, and elbows showed gross rheumatoid changes. Radiographs revealed erosion of the joint surfaces of the knees. His E.S.R. was still 100 mm. and the red blood cells numbered 2,300.000, with Hb 40%.

On admission after the haematemesis he appeared almost exsanguinated, and lay feeble and dazed. He was much wasted, and his knees were fixed in flexion. The other joints mentioned above showed gross rheumatoid changes. The heart was not obviously enlarged ; there was a blowing apical S.M. The pulse rate was 130, and the B.P. 85/35. The chest and abdomen were normal. The liver and spleen were not felt. The urine showed a heavy cloud of albumin.

He was immediately transfused with 2 pints (1.14 litres) of blood, and a further 2 pints was given four days later. The melaena gradually ceased and the haemoglobin rose to 62%.

Four weeks later (May 24) the patient's condition again began to deteriorate ; his throat became sore and his breathing laboured ; he complained of retrosternal discomfort, and was unable to sleep. The tongue was dry and smooth ; small red vesicles appeared in the sacral area. The haemoglobin was now 54%.

On the 25th he was much worse—drowsy and breathing deeply and rapidly (28). His pulse was 80 and B.P. 108/55. There were petechiae in the throat, and the spleen was just palpable. The urine now contained more than 1% of protein with a few red blood cells, but no casts. The blood urea was over 500 mg. per 100 ml. The patient died in uraemic coma that evening.

Post-mortem Examination (*Dr. J. L. Hamilton-Paterson*).—A moderately nourished man. Marked contraction of knees and hips as a result of old rheumatoid arthritis. Rheumatoid deformities also of hands and fingers. Heart : No abnormality apart from an old adhesive pericarditis. Lungs : Early right lower lobe bronchopneumonia. Liver enlarged and showing obvious diffuse amyloidosis on section. Spleen average size ; no macroscopic amyloid. Kidneys enlarged and adherent to perirenal tissues ; cortex grossly narrowed and pale ; medulla apparently normal : changes very suggestive of nephrosclerosis following amyloid disease. Alimentary canal : Stomach and duodenum normal ; small intestine showed patchy distribution of oedema and submucous petechial haemorrhages ; large intestine contained tarry blood ; gross congestion and oedema of mucous membrane at irregular intervals, but no ulceration : appearances those of uraemic inflammation. All other organs were normal.

Microscopy showed diffuse amyloidosis of the liver (Plate Fig. 2), glomerular and tubular amyloid degeneration of the kidneys (Fig. 3), and slight amyloid degeneration of the spleen (Fig. 1). The heart showed fibrinous pericarditis, and some cellular infiltration of the myocardium with histiocytes and eosinophils.

Discussion

The amyloidosis of rheumatoid arthritis is of the secondary type involving the kidneys most frequently, next the liver and spleen, and less often the suprarenals, lymph nodes, and intestines. The kidneys, and more rarely the spleen, may be involved alone. Hadfield (quoted by Hill, 1948) has described amyloid as "a structureless glycoprotein found in the tissues as an insoluble gel, and first appearing between the scanty cells of the endothelial lining of the capillary blood vessels." It lies outside the cells, greatly thickens the blood-vessel walls, and steadily progresses to cause great enlargement and translucency of the affected organs.

Its mode of development has provoked much discussion, and some authors—for example, Reimann and Eklund (1935)—bearing in mind its association with chronic infections, malignancy, and multiple myelomatosis, diseases in which the blood-protein levels are disturbed, would attribute it to an increase in the normal or abnormal blood globulins. If rabbits are injected with casein amyloidosis develops after the blood globulins have been doubled or quadrupled. But renal amyloidosis can also be produced in rabbits by injecting such varied substances as bacterial toxins (Boyd, 1947) and subcutaneous manganese chloride (Butt, 1930).

Reimann and Eklund support their view by quoting the observations of Langstein and Mayer (1903), who found that animals treated with vaccines developed amyloidosis. They feel that human beings receiving vaccine therapy may develop excess amounts of normal globulins or new abnormal proteins, and that these may be deposited in the tissues and converted into amyloid. But it must be emphasized that while cases with raised blood globulins and amyloid disease, like Case 1, are not infrequent, review of other described cases of secondary amyloidosis shows no constant relation between the development of amyloid and the level of the blood globulins (Trasoff *et al.*, 1944 ; Rosenblatt, 1933). A relative globulin increase is of course a secondary finding where renal amyloidosis has led to heavy albuminuria. Many cases of amyloidosis have had neither vaccine therapy nor chrysotherapy, the latter being implicated by Doubrow (quoted by Reimann and Eklund, 1935) as a possible cause of amyloidosis.

The described cases of rheumatoid disease have always been severe examples of the condition, usually much

emaciated and often anaemic as well, before they developed recognizable amyloidosis. The disease has also nearly always been protracted before the amyloidosis became apparent, though in a recent case the latter condition was recognized only eight months after the onset of the arthritis (Lush, Chalmers, and Fletcher, 1948). This combination of length and severity of the primary disease suggests that in rheumatoid and rheumatic disease, as in tuberculosis or suppuration, the toxins of the infection cause the amyloidosis. Eagles and his co-workers (1937) stated that the same virus causes both acute rheumatism and rheumatoid arthritis; and Mervyn Gordon (1948), in supporting this view, has pointed out that the fibrinoid degeneration of acute rheumatism may progress to amyloid degeneration. Beattie's cases of rheumatism, mentioned early in this paper, also seem to support this statement—as does the case of Imrie and Aitkenhead (1939) in which rheumatic fever led, after several years, to Still's disease and fatal amyloidosis.

Goldthwait (1940) has reported amyloidosis in 21% of the cases of rheumatoid arthritis which he has examined at necropsy, while Lush *et al.* found only one case among 200 rheumatoid arthritics examined in a clinic. The discrepancy between these two findings is accounted for both by the difficulty of recognizing amyloid disease in life and by its greater incidence in protracted and terminal cases; but the true rate of incidence evidently lies nearer to Lush's figure than to Goldthwait's, because of the many mild or moderate cases of rheumatoid arthritis which recover and in which there is no likelihood of amyloidosis.

Pathology

Secondary amyloidosis, with which this paper is concerned, differs from the primary amyloid disease sometimes seen in the tongue, alimentary tract, heart, and pericardium, in which no preceding cause is to be found, and in which not only the distribution of the amyloid substance, but also its composition, is different from that seen in secondary amyloidosis (Reimann *et al.*, 1935; Baber, 1947; Findley and Adams, 1948). But the exact composition and mode of formation of the amyloid is not fully known in either type. It is probably formed locally from connective-tissue elements (Warren, 1930), and I am indebted to my colleague, Dr. J. L. Hamilton-Paterson, for the observation that it probably represents a pathological change in the connective-tissue ground substance.

In the secondary type of disease deposition occurs generally in connective tissue and especially between and beneath the endothelial lining cells of the capillaries—for example, in the renal glomeruli (Fig. 3). The glomerular changes are responsible for albuminuria and, if extensive enough, for the one fatal result of amyloidosis, uraemia (Rosenblatt, 1933). Rosenblatt thinks with Fahr that in this disease the tubular degeneration is a proportional result of the glomerular damage. The cells are first swollen and contain fatty droplets (" amyloid nephrosis ") ; later there is marked atrophy. The only direct involvement of the tubules by amyloid is a slight and scattered deposition on the basement membranes (see Fig. 3).

Rosenblatt, whose cases were mostly victims of tuberculosis, found that out of 125 there were 87 (70%) showing renal involvement. Of these, 34% showed amyloid nephrosis and had a corresponding history of marked albuminuria and oedema. By contrast it is interesting to note that our second case showed renal contraction and marked uraemia and gave no history of an oedematous phase in his illness.

In Rosenblatt's series the spleen was involved most frequently—in 108 instances (88%); the liver was involved in 76 (60%); and the adrenals in 50 (40%). In no other organ or tissue was there any incidence in any way comparable to that found in these four sites.

When the spleen is involved it shows, as did Case 2, an involvement of the walls of the arterioles of the Malpighian bodies (Fig. 1). In this case the spleen was only lightly affected, but the liver changes were heavy (Fig. 2); and here again the deposits were in the characteristic place—in the connective tissue between the sinus endothelium and the liver cells, the latter being compressed by the larger deposits.

Diagnosis and Prognosis

A sufficient number of cases of amyloidosis in rheumatoid arthritis have been described during the past 20 years to suggest that this complication of rheumatic and rheumatoid disease will be recognized more often if it is always suspected when the condition has lasted over a year and has been severe enough to have led to marked loss of weight and to anaemia. Since the kidneys are most frequently and most seriously involved, albuminuria with hyaline and granular casts may be the best pointer. Hill (1948) has suggested that a " nephrotic syndrome " is a likely development, and claims that both nitrogen retention and hypertension very rarely develop in rheumatoid renal amyloid disease. Trasoff *et al.*, however, report that nine out of their 13 cases showed terminal uraemia. The rarity of hypertension in renal amyloidosis (Rosenblatt) and Hill's emphasis on the frequent, if often delayed, appearance of oedema in this condition are noteworthy. Oedema does not always occur in renal amyloidosis (for example, Case 2), though it is frequent and always to be expected when the serum albumin and total protein levels have been much lowered by albuminuria. The liver and spleen are also often involved by amyloid changes, and so hepatomegaly or splenomegaly, alone or associated, may be evidence of the disease. Case 1 suggests that liver biopsy is a safe, easy, and reliable diagnostic test when a large firm liver appearing in rheumatoid arthritis has suggested amyloid disease. Very occasionally, as in the case of Lush *et al.*, biopsy examination of enlarged lymph nodes occurring in rheumatoid arthritis may first show the amyloid disease.

The injection of Congo red, or the Paunz test, though not without risk, gives useful though variable information (Trasoff *et al.*). The test may show 90% retention of the dye in the first hour, but it is known that, exceptionally, cases of amyloid disease have shown as low a figure as 40%. A retention level of 65% is very suggestive of secondary amyloidosis. In primary amyloidosis where the " inmature " amyloid does not absorb the dye (Reimann *et al.*) the test has no value.

Prognosis is most grave when nitrogen retention occurs; marked oedema, whilst a serious matter, is not of itself fatal. Gross hepatomegaly and splenomegaly due to amyloidosis have of themselves no direct influence on the eventual course and outcome of the primary disease.

Treatment

First treatment of secondary amyloid disease is to eliminate the causative complaint. An empirical form of therapy with oral whole liver extract has also been tried in recent years.

The effective nature of the first line of treatment was well shown in an adult with a tuberculous empyema complicated by severe renal, splenic, and hepatic amyloidosis. In the three years following effective drainage of the empyema the amyloidosis appeared to clear entirely (Rosenblatt, 1936). In a similar period Walker (1928) observed complete regression of gross amyloidosis of liver

and spleen in a small boy after his chronic post-pneumonic empyema had been closed by thoracoplasty. Sherlock (1945), by liver biopsy in a case of chronic diarrhoea due to an unexplained ileo-sigmoid fistula, found that after two years her patient had gained weight despite continued moderate diarrhoea, and that his amyloid infiltration was considerably "less coarse."

Liver therapy cannot be said to have benefited any of these cases, though it was given during convalescence by Rosenblatt, but in the cases of Trasoff *et al.* (1944) and of Kennedy (1935) it may have had some good effect.

Summary and Conclusions

Two cases of rheumatoid arthritis complicated by amyloid disease have been described. Although there is uncertainty about the mode of production of this disease, it is noteworthy that in both cases the rheumatoid condition had been protracted and had caused pronounced wasting and anaemia as well as crippling joint changes.

In one case the disease had brought about blood-protein changes, only partly attributable to the severe associated albuminuria.

It is suggested that the amyloid-tissue changes are not due to the blood-protein changes, but that both are attributable to the rheumatoid infection.

Each case had had moderate gold therapy, but this probably had no bearing on the development of amyloidosis.

It is noted that one case, in spite of gross hepatic enlargement, splenomegaly, and marked albuminuria, shows no deterioration. The other patient died in uraemia, the only way in which amyloid disease can directly cause death.

Where the liver is enlarged, liver biopsy may be used with safety to establish the diagnosis.

Treatment with whole liver extract has so far had no definite effect on the amyloid deposits.

It is suggested that secondary amyloidosis is dispersed only after cure of the primary complaint.

It will be interesting to observe the effect of cortisone on the amyloid changes due to rheumatoid arthritis.

I am indebted to Dr. K. M. Lawther, of Middlesex Hospital, for details of the early course of the illness in Case 2, and to my colleague, Dr. L. I. M. Castleden, for the later notes on the same case. I am grateful to Dr. J. L. Hamilton-Paterson for help with the investigations and histology in these two cases, to Miss M. H. Shaw for the preparation of the photomicrographs and the photograph of Case 1, and to Dr. G. M. Barrett for the liver biopsy specimen from the same case.

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MEDICAL ADMINISTRATION IN THE TROPICS

BY

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Medical administration in the Tropics presents certain special features of its own. The climate, the prevalence of debilitating and often fatal communicable diseases, the effects on health and social life generally of economic development on the one hand or economic stagnation on the other, and, in many instances, the customs and beliefs of the general population in regard to diseases and their causation, all combine to produce conditions which differ in many important respects from those met in the more organized countries of temperate climates.

The situation in Tanganyika Territory after the 1914–18 war serves to illustrate the problems which face a medical service dealing with primitive conditions, while that in Trinidad and Tobago, with well-organized industries and more than a century of medical services, provides examples of the problems met in a comparatively advanced country.

Health Conditions and Medical Services in Tanganyika Territory

When the British took over the administration of German East Africa, as Tanganyika Territory was then, the effects of war were so devastating that, though some hospitals and laboratories were available and a number of trained dressers still remained, such medical services as the German Government had developed had almost completely disintegrated. The war was followed by a pandemic of influenza and by extensive famines.

As the British civil administration replaced the military occupation a medical department was gradually built up But even in 1921 a medical officer, assisted by a few sub-assistant surgeons, compounders, and dressers, might find himself responsible for the public health of a quarter of a million people, or even (though rarely) half a million. Such a service could touch only a fraction of the population, and indigenous forms of medicine and public health were widely practised. How effective the herbal remedies were it was hard to assess. It was rarely possible for an outside observer to study individual patients who were under treatment, and even more difficult to get to know the remedy used, as the "trade secrets" were closely guarded. For example, claims of success were made in the treatment of gonococcal infections, and there were apparently some grounds for the claims.

The abandonment of a house after one or more deaths had taken place in it seems to have been a common practice, and there may have been occasions when the custom was of benefit as a public health measure. The circumstances in which I saw the abandonment of houses most in evidence were during a sleeping-sickness epidemic, and the consequences were the opposite of salutary in that the effect was to spread the disease over thousands of square miles. Variolation was another common practice, and it is not improbable that it contributed to the dissemination of infection.

Witchcraft played its part in the sphere of health. It was, for example, apparently believed over a wide area

that leprosy was transmissible either by heredity or by means of witchcraft. Contact with a leprous case, no matter how close and continuous, was therefore not feared. It can easily be seen how such a belief would interfere with any measures of leprosy control. An even more sinister form of witchcraft manifested itself when it was believed that the death of a person was the work of an enemy practising witchcraft. When the guilty person was "discovered" it became a public duty to destroy him (or her). A number of known murders, even in recent years, were committed as a "public duty" of this nature.

The Medical Department

It was among beliefs and practices of this kind, differing in detail in different areas, that a medical officer carried on his work in the early days of the British administration. The medical department of that time consisted of a headquarters, a laboratory service, a central medical store, a number of station units, one or two medical officers for town and port work, and a dental officer.

The headquarters staff comprised a principal medical officer (a designation afterwards changed to director of medical services), a deputy principal medical officer (afterwards changed to deputy director of medical services), a senior sanitation officer (afterwards changed to deputy director of sanitary services), and their clerical staff. Early in the history of the department the principal medical officer became, *ex officio*, a member of the Executive and Legislative Councils. In addition to these and various other duties he also became President of the Medical Registration Board and Chairman of the Central Town Planning and Building Committee. This committee was given statutory powers to regulate building in townships. In the districts the Central Committee was represented by subordinate committees, the medical department's representative on them being the station medical officer or medical officer of health.

The laboratory service carried out public health bacteriology (including water sampling), clinical pathology, medico-legal work, and the production of various vaccines. There was no chemist attached in the first instance, but a chemistry section was added later.

The central medical store was the distributing unit for medical supplies.

The station units were the basic units of the department. One unit was usually under the direction of a medical officer (the station medical officer), who was assisted by one or more sub-assistant surgeons, and by compounders and dressers. Some of the more important units were placed under senior medical officers, and there were a number of sub-units, usually subordinate to the medical officer or senior medical officer of a full unit, which were placed under sub-assistant surgeons, compounders, or dressers. The head of a station unit was directly responsible to the Principal Medical Officer. The unit headquarters were always, or nearly always, at the administrative headquarters of a district. The medical officer was usually given a small station hospital to work, and he conducted, in the station and in the district, such sanitary and other public health activities as he was able to undertake. One of the simplest of these—because it could be carried out by dressers and other subordinate staff—and one of the most important, was vaccination against smallpox.

Problems of Administration

In the early days of the administration little systematic survey work could be done, but the Service was able to get some indications of the problems with which it had to deal from the records of work carried out by the former German administration, from cases observed at the station hospitals, from the sanitary conditions found in the stations themselves and in places visited outside them by the medical officers, and from reports received through district administrations, chiefs, and other persons. It was found that helminthic diseases, malaria, relapsing fever, and venereal diseases (following in the wake of trade and war) were widespread; the dysenteries, leprosy, schistosomiasis, tropical ulcer, yaws, and many of the general diseases were common; anthrax, sleeping sickness, smallpox, tuberculosis, and sometimes plague (bubonic) occurred in places. At the end of 1921 there were 23 station medical officers (including senior medical officers and medical officers of health) and 21 sub-assistant surgeons, with their ancillary staffs, to deal with this assortment of diseases in a country over 350,000 square miles in extent; moreover, the mental attitude of the general population towards the various conditions complicated the work. The few mission and private practitioners in the country concerned themselves almost entirely with individual cases, except that some missions gave considerable assistance in looking after leprosy settlements.

The central administration was able to give some direction on policy and on specific public health measures and to carry out a limited amount of inspection, but the medical officers, especially in the more remote districts, had to rely largely on their own initiative and judgment. This organization, while allowing scope for initiative, militated against the development of co-ordinated public health policy—all the more so as medical officers might serve for no more than two to two and a half years consecutively in the one station. This weakness was partly eliminated by the formation of special units, and, later, by the introduction of a provincial system of medical administration. The first special unit to be formed was the sleeping-sickness control branch, which began work in 1926. The necessity for this branch arose from the fact that Rhodesian sleeping sickness had, for the first time on record, now appeared in epidemic form. One of the features of this unit was the opportunities which it provided for interdepartmental collaboration. People had to be settled on new land, usually in tsetse bush, and problems relating to native beliefs and customs (provision had sometimes to be made even for the transfer of an ancestral spirit), district administration, and agriculture were nearly always involved, and the Department of Geological Survey had sometimes to be consulted on water supplies.

Later on, research units for sleeping sickness (distinct from the executive unit), malaria, and tuberculosis were formed. They all proved valuable to the Service because of the investigations which they were able to undertake and the guidance they were able to give to medical officers and medical officers of health. Special interest attaches to the work of the sleeping-sickness research unit, which showed that the trypanosome of Rhodesian sleeping sickness could pass from man through tsetse, game animal, and again through tsetse, and remain infective to man (Corson, 1935). The possibility of this cycle taking place could be shown only by experiments on human volunteers, the first of whom was the experimenter himself.

Other units of a different kind which were formed included an institute for the production of calf-lymph smallpox vaccine, and a training school for dispensers, who, in addition to dispensing, were taught the diagnosis (including microscopical diagnosis) and treatment of some common diseases.

The introduction of a provincial medical administration was necessarily preceded by the formation (in 1925–6) of provinces, in each of which the provincial commissioner was the representative of the central Government. In the provinces there were native authorities, responsible to the provincial commissioner and his district officers,

who administered native law and customs within certain prescribed limits.

The provincial medical officers, when their posts were created about ten years after the formation of provinces, administered the medical and public health services in these provinces. They were the responsible advisers to the provincial commissioners on health matters, but were directly responsible to the Director of Medical Services in both technical and administrative matters.

The rudiments of a Native Authorities' medical service came into being with the introduction of tribal dressers. These dressers were trained in the Government hospitals, but after training came under the administration of their own Native Authorities, though Government medical officers gave them a certain amount of supervision in an advisory capacity. Their standard of efficiency was very low at first, but they were the beginning of a service which may eventually be a useful one under local governments.

The dental service remained a branch of the medical department throughout, but even in 1938 it was still limited to two regular officers and a dental mechanic.

This review of the Tanganyika medical administration covers the period up to 1938 only. During these years the declared policy of the medical department was virtually controlled by the Director, subject only to the limitations set by finance and to the provisions of infectious diseases and other relative ordinances. He continued to preside over the Board responsible for the registration and professional discipline of medical practitioners, and the members of the Board were, in practice, nominated by him. He ceased to be an *ex officio* member of the Executive Council, but continued on the council as a nominated member, and also continued to be a member of the Legislative Council. He had his own staff, administrative and executive (including, by now, specialists in medicine and surgery), available to advise him, but there was no standing advisory committee or board of health to advise or assist him.

Fuller information on the organization of the medical department may be obtained from its annual reports and from the ordinances relating to public health and town planning and building.

Medical Administration in Trinidad and Tobago

Medical administration in Trinidad and Tobago has undergone considerable changes since the inception of medical services in these islands. An interesting history of those services, covering a period of 130 years, has recently been written by Dr Roul Seheult (1948), a former resident surgeon of the Colonial Hospital, Port of Spain.

The administrative system as it was in 1947 consisted of certain statutory bodies which were responsible for the administration of laws relating to public health and to the professions of medicine, dentistry, pharmacy, and midwifery; of a health department of the central Government; and of certain health services provided by municipalities.

The chief statutory bodies are the Central Board of Health; the local health authorities, which are subordinate to the Central Board of Health; and the Medical Board of Trinidad. There is also an advisory committee, not a statutory body, which advises the Director on matters of policy.

The functions, powers, and the duties of the Central Board of Health are laid down in the Public Health Ordinance of Trinidad and Tobago. The Board has wide powers for the control of infectious diseases; it can frame model by-laws, approve or refer back for revision any by-laws submitted by a local health authority; and it has discretionary powers in respect of the erection of and repairs to buildings. The by-laws framed or approved by the Board must receive the approval of the Governor in Council and be published in the *Royal Gazette* of the Government before they come into force. The Director of Medical Services is, *ex officio*, chairman of the Board; its members, who are partly official and partly non-official, are appointed by the Governor.

The local health authorities are, under the Board, responsible for their respective areas, which correspond to the different administrative units—municipality or county—of the Colony. In the municipalities (city or county, as the case may be) the council, an elected body, comprises the local health authority. In the counties the chairman and members were up to 1947 appointed by the Governor.

The local health authorities may prepare by-laws and submit them for approval to the Central Board of Health. They are responsible for seeing that the Public Health Ordinance and the by-laws made under it are complied with. They grant certain licences and issue certain permits, and they exercise such special powers as may be delegated to them by the Central Board of Health.

In the city of Port of Spain, the city council, which is also the local health authority, has its own medical officer of health and sanitary staff. The medical officer of health is not in this case responsible to the Director of Medical Services except in so far as the local health authority to which he is the expert adviser on public health matters is responsible to the Central Board of Health, of which the Director is chairman. In the case of the borough councils the medical officers of health are seconded from the Health Department of the central Government and, though directly responsible to the borough councils for administrative purposes, they remain under the technical direction of the Director of Medical Services. In the counties the medical officers of health are responsible to the Director of Medical Services or his local representatives in both administrative and technical matters.

The Medical Board of Trinidad has its functions, duties, and powers laid down in the Medical Board Ordinance. It is composed of all the registered medical practitioners of the Colony, and its council, appointed by the members from among themselves, is responsible for the professional discipline of members of the professions of medicine, dentistry, pharmacy, and midwifery. It also provides for the registration of medical and dental practitioners; it conducts examinations for, issues licences to, and registers candidates for the three other professions; and it has certain other duties.

The present functions of the Health Department are not defined by statute or by Government regulation except to a very limited extent (e.g., the Director and some members of his staff have certain *ex officio* duties), though these functions are largely a growth from the early obligations undertaken by the Government to provide medical care for the indigent and to control acute infectious diseases.

Its organization consists of a headquarters and a number of units, each of which is directly responsible to the Director. The main units are the county health services; the specialist units comprised by the leprosy, malaria, tuberculosis, and venereal diseases divisions; the general hospitals, providing specialists in medicine, surgery, and midwifery, with radiology and radiotherapy in some; the houses of refuge (combinations of workhouses and infirmaries for chronic indigent cases); the central laboratory, carrying out clinical

pathology, public health bacteriology, and the production of vaccines; the central medical stores; and the dental service.

The county health services are the basic units of the department. As these units are designed, each county should have its own separate service, but shortage of staff has necessitated the placing, in some cases, of several counties under a senior medical officer of health. County health work groups itself into five main categories—namely, advice on town and village planning; the control of communicable diseases, where this is not undertaken by specialist units; medico-legal services; family welfare services, especially maternity and child welfare, school medical services, nutrition, and health education; and services for general diseases and injuries, including, in some places, in-patient treatment. Some services, like applied health education, are still in their infancy, and some, like the school medical service, are still inadequate. The counties do not have their own specialist services. Cases requiring medical or surgical specialist treatment are sent to the general hospitals, and the specialist units deal with major problems in their particular specialty.

This review of medical administration in Trinidad and Tobago refers to conditions as they were in 1947. It will be seen that organized unofficial responsibility in matters of public health and professional discipline had proceeded there much further than it had in Tanganyika Territory just before the 1939–45 war. The Colony of Trinidad and Tobago had also relatively a much larger staff. At the end of 1946 its establishment of registered medical practitioners in the health department, including specialists and officers carrying out administrative duties, was 101 (though actually a large number of posts were vacant), whereas at the beginning of 1939, in Tanganyika Territory with a population of about 5,500,000—more than eight times that of Trinidad and Tobago—the establishment of registered medical practitioners was 50, and of the various grades of assistant and sub-assistant surgeons 55. Besides, probably there were relatively more private practitioners in Trinidad and Tobago than in Tanganyika.

Present-day Trends and Needs

The changes that are taking place in the outlook and modes of living of tropical peoples, the expansion and increasing complexities of social services, and, in some countries at least, the growth of representative government have all produced a tangle of trends and needs which complicate the duties and problems of medical administration and call for new orientations.

If the growing demands for satisfactory standards of health and the growing readiness to provide the means are to be implemented the general population must be taught the parts which they have to play in order to attain them, and their representatives and leaders must learn the principles and the liabilities involved. Medical administrators themselves should be selected early in their careers and given facilities for special training; and there must be adequate direction and control.

The training of any people on a large scale in healthy living and health discipline is not an easy undertaking. The task of disseminating health education which will be of practical value in primitive communities is a gigantic one, and the time and continuity of effort required to make a success of it can be appreciated only by learning something of the deep-rooted traditional beliefs which exist in tropical countries about the causation and significance of disease. These beliefs have to be replaced by genuine knowledge, and the old customs which are not compatible with it replaced by new habits and standards of living. It is a problem which has to be faced, and it is by no means a hopeless one. The main objectives are definite enough: the blending of health habits and attitudes with day-to-day activities; the imparting of such knowledge and the inculcation of such sense of responsibility as may be necessary for healthy living in a way in which their application to everyday life may be understood and practised; and the healthy cultivation, or at least the maintenance, of the primitive faculty of intuitive interpretation of bodily symptoms—a necessary safeguard against the hypochondriasis which may follow on a misguided interest in disease.

Even among the more sophisticated, who might be expected to be the interpreters of health education to their simpler neighbours, there are obvious difficulties in the case of people with traditions which are quite alien to our own. There are, for instance, the contradictions in the teaching given in the semi-pagan home or neighbourhood and that given in schools and clinics; and conflicts, which may even lead to neuroses, may develop where religious teaching is at variance with current opinions and practices. For this and other reasons, as life in the Tropics becomes more complex so the practical aspects of the neuroses are likely to become more apparent. They are responsible for a large amount of invaliding now among the more sophisticated and less stable communities, and it may well be that medical administrations will have to give as much attention to their general predisposing causes as they now do to the control of communicable diseases. (It is not only in the subconscious minds of patients that conflicts may take place. The role of the medical administrator may be particularly difficult when he tries to collaborate, as he must do, with educational authorities and religious workers. Those who have had no practical experience of such associations should be able to see, from even a superficial acquaintance with some of the modern literature on social and psychological medicine and with some social workers, how delicate the position can sometimes be.)

If, as it should do, health education is to play a significant part in the attainment of bodily and mental health in the Tropics it is evident that investigations will have to be carried out to see how best to teach and how best to assess results. Such investigations cannot be carried out just as part of the routine work of an educationist or a public health officer; expert knowledge on social anthropology and on psychiatry is essential as well.

A Growing Tendency

With the growth of more representative Government in the British Colonial Empire there is a growing tendency for lay representatives and administrators to control, or at least influence, the direction of medical and public health affairs. The success of more lay control in health matters will depend very largely on the success that is obtained with the health education of the general public in practical matters and on the extent to which their representatives and leaders accept the teaching given and grasp the social and economic significance of the major diseases and the financial and administrative implications of their treatment and control.

Health information must be made available to lay administrators and councillors which will deal with current health problems as they present themselves year by year, with the economic and social repercussions of prevailing diseases, and with the practical measures that must be taken to improve medical facilities and raise standards of health.

In preparing information of this kind it is essential that medical administrators should be placed in a position of

sufficient independence to enable them to present facts and professional opinions regardless of their political or commercial implications.

As lay influence increases outside the departments it will provide some supervision of a kind that may be helpful, but not such as will meet departmental needs. Medical work expands comparatively rapidly in the Tropics, and supervision and assessment of work tend to lag behind the increasing routine executive work, with the result that the actual work of a department may grow to be at variance with the policy which it is expected to implement. To avoid this a closer linkage than exists at present is needed between executive and administrative staffs, and the latter must be given the time and facilities to keep in practical touch with all aspects of departmental work.

The services which have been outlined—the health education of the general population, the provision of special informatory facilities for lay administrators and councillors, and the extension of follow-up and inspectoral services—are vital to British Colonial medicine, and, as a corollary, the administrators who will have to put them into effect will have to be trained for the task.

Need for Special Training

Whatever developments there may be in private practice in the Colonial Empire, there will always be a large volume of medical work which must be done by the health services of the central or local governments, and it should be recognized that special training should be made available for medical administrators. The duties of a station or district medical officer are, on a small scale, analogous to those of the head of a health service and his staff. Training in administration can therefore begin with the medical officer, who has sanitary, medico-legal, and general medical duties to perform.

Much of the medical work now needed in the Tropics, if it is to be productive, must be planned on a scale which requires several years for its completion, and medical officers should be encouraged to draw up their own schemes of work and to co-operate, within the framework of a general departmental policy, with other departments and organizations of related interests, especially education, agriculture, engineering, and such bodies as are concerned in social and moral welfare. It is not expected that every medical officer should operate a miniature medical department, but a selected proportion who show initiative, readiness to accept responsibility, and an aptitude for leadership and for administrative work generally should be given every opportunity, by way of study leave and conditions of work, to widen their knowledge not only of medicine itself but also of its relations with social and economic welfare.

In addition to the ordinary postgraduate courses which are available in tropical medicine, general medicine, public health, etc., there should be arrangements for selected candidates to be given special courses designed to provide the wider outlook which is now required in tropical social medicine. These should include the nutritional aspects of such agricultural subjects as soils and soil microbiology, fertilizers, animal feeding, dairy chemistry, storage of food crops, etc.; studies in education and sociology, comprising social psychology and educational psychology; and studies in psychiatry, including social psychiatry and mental hygiene. The medical officers should also, as opportunity permits, engage in some research, receiving guidance and criticism from an experienced research worker. Officers who continue to maintain those wider contacts for a long period obviously cannot specialize, or at least can do so only in a very narrow field. They should, nevertheless, so long as they maintain touch with clinical work, continue to be practical diagnosticians in such a way as will enable them to use and assess the services of specialists. This advanced general training prepares them for passing on from district, sanitary, or hospital work to take administrative charge of the health services of a county or province as the case may be. Another opening that should be available to them is hospital administration where the number of in-patients is large enough.

It is still debated whether the officer administering a hospital should be medically qualified or a layman. In Colonial medical administration there are great advantages in appointing a medical officer as administrator, provided he makes administration his primary duty, keeps touch (not as a consultant but as an administrator) with his officers' clinical work, and maintains with district work the contacts which make his hospital a unit in a larger team. He should be assisted by a lay administrator. Medical officers who receive the advanced training and have gained the special experience which has been outlined should be well equipped for the most senior administrative posts. These medical officers will be unable to keep their professional knowledge up to date unless they are provided with summaries for reference. These should be in the form of "digests" of what is known of the particular subjects at the time; they should not be précis of recent work. They could be compiled in loose-leaf form, and should show the latest state of knowledge, year by year, of the whole field of medicine. (An example of a reference book of the kind required for a particular subject, which is already available, is Martindale's *Extra Pharmacopoeia*.)

If medical administrators are to keep this close touch with their own and allied professions it is obvious that lay assistance of a first-class order must be developed to manage the details of lay administration within their department.

Summary

A short outline is given of medical administration and organization as it was in Tanganyika Territory before 1939 and in Trinidad and Tobago in 1947.

The advances made in the development of representative Government in the British Colonial Empire throw new responsibilities on medical departments, which should now accept it as one of their major functions to see that the representatives and leaders of the people are kept fully acquainted with the social and economic effects of the important prevailing diseases, the measures that can be taken to prevent or attenuate them, and the community discipline, in habits and behaviour, which is necessary for sound standards of health. Similarly, the medical departments must, as a long-range policy, play a major part in guiding the people themselves to a wholesome mode of living. These functions imply that there must be investigations—not necessarily by medical departments alone—into social structures and their inherent customs and practices.

Opportunities should be provided for medical officers of suitable calibre to engage both in work and in special duties which will equip them for supplying the directives and guidance which will be required of organized medical services. Medical administrators need more facilities for special studies than are now readily available for them. They must also have better facilities for the supervision and assessment of the work of their departments if the best results are to be obtained and misapplication and wastage of resources are to be avoided. As new and increasing demands are made on them because of the widening application of social medicine, as much as possible of routine non-professional administration must be delegated to laymen.

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A TRIAL OF PROCAINE PENICILLIN PREPARATIONS

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It now seems likely that for some time to come procaine penicillin will play an important part in penicillin therapy. The first paper describing its clinical use (Herrell, Nichols, and Heilman, 1947) advocated a dosage of 300,000 units in oil, this amount being contained in a total volume of 1 ml. Although a satisfactory clinical response was claimed with this dosage at the time, and by other authors subsequently, it has been criticized on the theoretical grounds that it would not provide throughout the whole of any 24-hour period detectable amounts of penicillin in the blood of all patients treated. Various preparations of procaine penicillin designed to overcome this drawback have been described, but as yet the majority of the reports have been mainly concerned with recording the blood levels obtained by their use.

This paper is an account of a trial of three preparations of procaine penicillin to determine whether any of them would satisfy the following criteria: (1) Provide a satisfactory preparation with which to treat acute staphylococcal infections of the skin and subcutaneous tissues, and, by analogy, infections due to more sensitive organisms. (2) Maintain detectable amounts of penicillin in the blood throughout 24 hours after a single injection. (3) Allow the dose to be given without difficulty in a volume of not more than 1 ml.

Preliminary Trials

Thomas, Lyons, Romansky, Rein, and Kitchen (1948) showed that the addition of aluminium stearate to procaine penicillin resulted in a slower release of penicillin from the site of injection and a consequent lengthening of the time during which penicillin could be found in the blood.

The first preparation tried by us consisted of 300,000 units of procaine penicillin in oil with 2% aluminium stearate contained in 1 ml., and this was used in the treatment of 24 patients with acute staphylococcal infections. This dose was given once every 48 hours, and penicillin was found in the blood of 22 of the patients after 24 hours and in the blood of 10 of the 11 patients tested after 48 hours. As reported previously, however (Griffiths, Jones, Shooter, and Heady, 1949), the clinical response was not as satisfactory as that seen with 300,000 units of procaine penicillin. No attempt was made to use this preparation in daily doses or in larger amounts, as the immediate response in the first 24 hours of treatment was thought to be less satisfactory than with procaine penicillin and it was not desired to increase the volume of the injection above 1 ml.

A similar series of 41 patients was treated with daily injections of a mixture of 200,000 units of procaine penicillin in oil with 2% aluminium stearate and 100,000 units of sodium penicillin, again contained in 1 ml. With this preparation penicillin was found in the blood of only 29 out of the 38 patients tested at the end of 24 hours; and, as the clinical results compared unfavourably with those in patients treated with 300,000 units of procaine penicillin, this preparation also was discarded.

The third preparation tested consisted of a mixture containing 300,000 units of procaine penicillin in oil with 1% of aluminium stearate and 100,000 units of sodium penicillin contained in 1 ml. Initial clinical trials of this preparation were satisfactory. We have attempted to compare its action in the treatment of acute staphylococcal infections of the skin and subcutaneous tissues with that of 300,000 units of sodium penicillin in saline given twice daily, and 300,000 units of procaine penicillin given once daily, and records have been kept of penicillin levels in the blood throughout treatment.

Methods of Treatment

Patients were given an intramuscular injection of 1 ml. of the trial preparation, and this injection was repeated daily for five days. As local treatment, sodium sulphate (12½%) and, in some cases, kaolin poultices were used, and immobilization of the affected part was advised wherever practicable. Only unavoidable and minimal incisions were made. Carbuncles were never incised. Most of the patients were examined at daily intervals, the remainder never less than once in three days. Clinical findings were recorded on a special form. As a rule a swab was taken from a lesion before the start of treatment or as soon as possible after pus had begun to discharge.

Conditions Treated.—Only out-patients with acute septic infections of the skin and subcutaneous tissues, mainly staphylococcal, who required penicillin were treated. The types of infection are given in Table I. Some of the

TABLE I.—*Types of Infection Treated (113 Cases)*

Boils	41
Cellulitis	22
Carbuncles (except dorsal finger carbuncles)	32
Dorsal finger carbuncles	5
Other conditions	13

TABLE II

	Mean Redness		Mean Induration	
	Present Series	Previous Series	Present Series	Previous Series
	in. cm.	in. cm.	in. cm.	in. cm.
Boils	1·9 4·8	1·4 3·6	1·2 3·0	1·1 2·8
Cellulitis	3·4 8·6	2·7 6·9	1·3 3·3	1·4 3·6
Carbuncles of neck	2·0 5·1	2·1 5·3	1·7 4·3	2·1 5·3
All carbuncles except dorsal finger carbuncles	2·2 5·6	2·1 5·3	1·7 4·3	1·8 4·6
Dorsal finger carbuncles	1·1 2·8	1·7 4·3	0·9 2·3	1·1 2·8
Other conditions	1·9 4·8	2·1 5·3	0·9 2·3	1·5 3·8
All conditions	2·2 5·6	2·0 5·1	1·2 3·0	1·4 3·6

Present series = Treatment with 300,000 units of procaine penicillin + 100,000 units of sodium penicillin and 1% aluminium stearate. Previous series in Tables II and III = Combined procaine penicillin and sodium penicillin series taken from the paper by Griffiths, Jones, Shooter, and Heady (1949).

patients did not complete the full course of treatment; these have been excluded from the series. Among the "other conditions" are included lesions not numerous enough to form separate groups, such as lymphadenitis and abscesses.

Severity of Infections Treated.—To allow adequate comparison between this series and previous ones, the same criteria of severity—the maximum diameters of redness and induration—have been adopted. The average for the various groups of lesions, compared with similar figures from the previous series, is shown in Table II. It will be seen that there is a close similarity between the two series at the start of treatment.

TABLE III

	Mean Time to Relief of Pain (Hours)		Mean Healing Time (Days)	
	Present Series	Previous Series	Present Series	Previous Series
Boils	31 (33)	26 (36)	7·3 (39)	8·0 (50)
Cellulitis	29 (19)	27 (15)	7·0 (21)	7·9 (27)
Carbuncles of neck ..	34 (9)	38 (10)	12·7 (10)	12·8 (17)
All carbuncles except dorsal finger carbuncles ..	34 (26)	29 (31)	12·8 (29)	13·2 (45)
Dorsal finger carbuncles ..	42 (5)	23 (13)	10·0 (5)	12·2 (13)
Other conditions	44 (7)	27 (54)	7·7 (13)	8·1 (83)
All conditions	33 (90)	27 (148)	8·9 (107)	9·4 (218)

The information was not available in every case, and the figures in parentheses indicate the number of cases on which the times were based.

Results of Treatment.—The results, again compared with those of the previous series, are recorded in Table III under the headings of relief of pain and healing time, defined as the time from the start of treatment to epithelization. The healing times are also shown diagrammatically in Fig. 1. No complications were seen in any of the patients, nor did any of them require to be admitted to the wards.

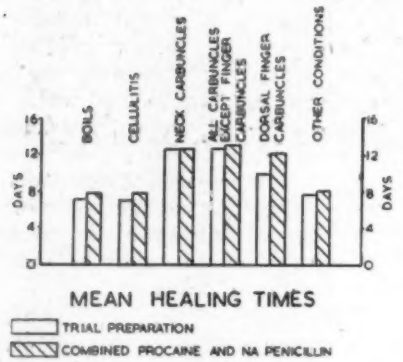

FIG. 1

Bacteriology.—All the swabs were sown direct on to horse-blood–agar plates in which two cups had been cut with a cork-borer. After inoculation the cups were filled with solutions of 10 units and 1 unit per ml. of penicillin. The results of these examinations are given in Table IV.

TABLE IV.—*Organisms Isolated from Initial Swabs*

	No. of Cases
Staph. pyogenes, penicillin-sensitive	65
" penicillin-resistant	3
Coliform bacilli	3
Haemolytic streptococci	2

Penicillin Blood Levels during Treatment.—Blood was taken from 81 patients when they attended on the second day of their treatment and before they received their second daily injection of penicillin. From these samples it was possible to estimate the amount of penicillin in the blood towards the end of the 24-hour period. The results are shown in Fig 2. Penicillin was assayed by the Oxford slide method, using the Oxford H staphylococcus. It will be seen that in 78 out of 81 patients detectable amounts of penicillin were present towards the end of the first 24 hours of treatment.

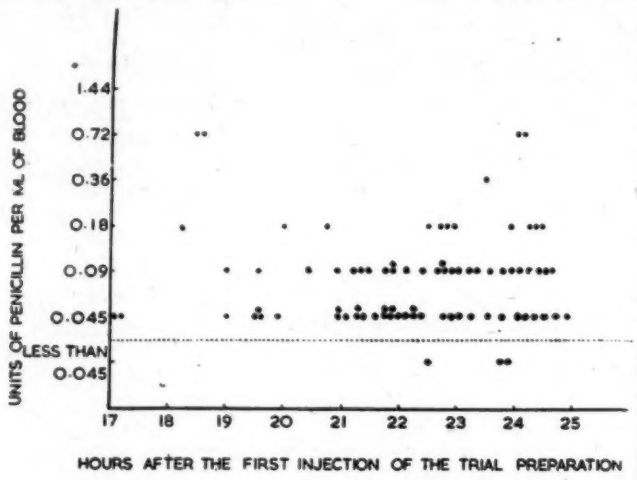

FIG. 2

Conclusions

From the results obtained and the clinical impressions during the course of the trial it would seem that this compound provides a form of treatment of acute staphylococcal infections which is as satisfactory as daily doses of 300,000 units of procaine penicillin, or twice-daily doses of 300,000 units of sodium penicillin in saline. As the figures agree so closely it has not been considered necessary to submit them to detailed statistical analysis.

This preparation also seems to provide detectable amounts of penicillin in the blood throughout most of the 24 hours in the majority of patients. This apparent advantage over treatment with procaine penicillin, in which a larger number of patients have periods of a few hours at the end of the 24 hours when penicillin can no longer be found, has not been shown to produce any markedly superior result. The explanation of this probably lies in the work of Eagle and Musselman (1949), who have shown that for many organisms penicillin has a bacteriostatic effect which persists for a number of hours after the removal of the drug. The therapeutic significance of this post-penicillin recovery period is enhanced by the fact that the recovering bacteria, damaged but not killed by the previous exposure to penicillin, are abnormally sensitive to the host's defences. In consequence the bactericidal process continues *in vivo* for some hours after the concentration of the drug itself has fallen so low as to be ineffective.

The explanation of our failure to achieve equally good results with 300,000 units of procaine penicillin with 2% aluminium stearate given once every 48 hours, or with 200,000 units of procaine penicillin with 2% aluminium stearate and 100,000 units of sodium penicillin given daily, apparently lies in the fact that effective concentrations were not reached for the treatment of such relatively walled-off lesions as the staphylococcal ones treated, though these compounds, in the dose used, might well provide adequate treatment for more amenable infections.

The final requirement, that the dose of penicillin should be given without difficulty in a total volume of 1 ml., was partially fulfilled. A moderately large needle is necessary with all the oily preparations at present available, and a certain amount of pressure has to be used in administration. This preparation compared favourably with any we have tried, but on grounds of convenience alone would be superseded by a preparation having similar properties but able to be injected easily through a hypodermic needle.

Summary

One hundred and thirteen patients with acute staphylococcal infections have been treated with daily doses of a preparation consisting of 300,000 units of procaine penicillin in oil with 1% aluminium stearate and 100,000 units of sodium penicillin. The results have been found to be as satisfactory as those in a similar series of patients treated with 300,000 units of procaine penicillin daily or 300,000 units of sodium penicillin in saline twice daily.

Levels of penicillin in the blood of 81 of these patients during treatment are recorded.

We would like to thank Professor Sir James Paterson Ross and Professor L. P. Garrod for their advice and criticism, Miss Deal, sister in charge of the surgery, and the nursing staff for their co-operation, and Miss M. Rhodes for technical assistance. We are indebted to Messrs. Glaxo Laboratories Ltd. for all the preparations of procaine penicillin used.

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CANCER OF THE UTERUS IN ADRENOGENITALISM

BY

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[WITH PHOTOGRAVURE PLATE]

Tumour formation is not uncommon in the course of adrenogenitalism, but the following case is unusual in that carcinoma of the uterus with the rare features of adenoacanthoma developed in the thirteenth year of illness.

Case Report

The patient, an unmarried woman aged 31, first reported to Professor A. P. Thomson's clinic in 1937. During the previous four years she had doubled her weight to 280 lb. (127 kg.), while menstruation had ceased in 1936. She was grossly obese and hirsute; her blood pressure was 170/110. Within two years a restricted diet with 2 gr. (0.13 g.) of thyroid a day reduced her weight to 145 lb. (66.8 kg.) and her blood pressure to 145/90. Normal menstruation restarted at the outset of treatment.

In 1942 her weight increased by 30 lb. (13.6 kg.) despite her reduced diet and 2 gr. of thyroid a day. She was given 3 gr. (0.2 g.) of thyroid daily, and this, with the work involved in nursing her father in a terminal illness, brought her weight to normal. For the first time, however, her general health then broke down. She was depressed and listless, and became fatigued on slight exertion. She also suffered from vertigo and bouts of left-sided headache.

First Admission

When admitted to hospital on July 21, 1943, the patient was mentally depressed and apathetic. Her face was highly coloured and she had marked generalized hirsuties and acne vulgaris. Visual fields, fundi, *x*-ray film of pituitary fossa, B.M.R., fractional test meal, and blood Wassermann reaction were all normal. Her weight was 148 lb. (66.7 kg.); serum chlorine ions, 359 mg. per 100 ml.; and serum potassium, 320 mg. per 100 ml.

Her condition was serious enough to cause anxiety, and Mr. H. H. Sampson, honorary surgeon, Queen Elizabeth Hospital, finally agreed to explore her adrenal glands. At a preliminary laparotomy an enlarged left adrenal gland was felt and a follicular cyst about the size of a hen's egg was removed. Ten days later the enlarged gland was removed without difficulty through a loin incision. Post-operative shock, often described after this operation, was absent.

The gland weighed 13.3 g. and consisted of diffuse cortical hyperplasia with areas of nodular hyperplasia of the zona fasciculata.

Result.—The most striking effect was the great improvement in the generalized acne vulgaris, and this may have contributed to her improved mental state. She became cheerful and regained her usual energy, returning to full work as a clerk. Four weeks before operation her 24-hour urinary androsterone level was 12.4 mg.—that is, within the normal range. Five days after adrenalectomy it fell to 4 mg.

Second Admission

On August 20, 1947, the patient was admitted to the University gynaecological unit on account of continuous uterine bleeding for the previous 12 weeks. She was grossly obese (220 lb.–99.8 kg.); hirsuties was pronounced over the face, areolae of nipples, and legs. There were mild acne vulgaris of her highly coloured face and many healed acne scars over her back and chest. Fat striae were present over the legs and abdomen, while the left tibial region had been swollen and oedematous for the past five months (Figs. A and B). Her voice was hoarse and croaking, but she asserted that this was normal.

FIG. A.—A single woman aged 41 with adrenogenitalism for 13 years. Weight variable, at present 180 lb. (81.6 kg.). Note the fat striae. The deep abdominal scar resulted from a mild infection of the very obese abdominal wall at hysterectomy.

FIG. B.—Same case as Fig. A. Marked hirsuties but without acne vulgaris. The hair is coarse and dry.

General examination showed that the systems and urinary analysis were normal. There was no obvious explanation for the swelling over the left tibial region. Her blood pressure was 160/80; pulse 72. Visual fields and fundi were normal; the red blood cells numbered 4,600,000; haemoglobin, 100%; white blood cells, 4,600; differential count, normal; B.M.R., minus 10%; radiographs of long bones revealed no osteoporosis; the pituitary fossa was normal.

The biochemical findings were as follows:

Blood chlorides (before operation)	359 mg. per 100 ml.
Serum sodium	318 " " " "
" " (15 months after operation)	286 " " " "
" chlorine ions (before operation)	369 " " " "
" " (15 months after operation)	372 " " " "
" calcium (after operation)	10·6 " " " "
" phosphorus	3·3 " " " "
" alkaline phosphatase	7·5 units " " "
Total calcium (1,631 ml. urine in 24 hours)	277 mg.

Gynaecological findings, apart from a bulky uterus, were normal, with female hair distribution and normal clitoris.

Operation (September 18, 1947).—After curettage had shown carcinoma of the uterus, total hysterectomy with removal of the remaining tube and ovary was performed. The uterus, which was 4 in. (10.16 cm.) long, was also bulky, chiefly owing to hypertrophy of the lateral muscular walls (1½ in.—3.8 cm.—thick). The postero-lateral wall of the uterus was infiltrated with an area of carcinoma 1 by 1 in. (2.5 by 2.5 cm.) in area.

On microscopy the myometrium was penetrated by masses of typical adenocarcinoma, through which were scattered areas of paler-stained cells (Plate, Fig. 1). These pale areas proved to be typical of adeno-acanthoma—that is, cellular metaplasia of glandular carcinoma gave a superficial (low-power) resemblance of cell-nests. Fig. 2 shows that the metaplasia affects both epithelial and stromal tissue. From the epithelial cells arise clusters of bizarre cells, irregular in shape and size, with pale-staining cytoplasm and nuclei containing little chromatin apart from fragments at the periphery. The stromal degeneration was of hyaline type.

Hormone Assays

These were made by Dr. A. M. Hain, of Manchester University. Two factors apart from hysterectomy could have influenced the readings: first, the patient has had 2 gr. of thyroid every day for the past six years; and, secondly, during the ninth month after operation she had 17,000 mg. of alpha-tocopherol (vitamin E) to control and finally cure her severe menopausal flushings. The readings are shown in the accompanying table.

Hormone Assays

	Pre-operative	2 Weeks Post-op.	15 Months Post-op.	17 Months Post-op.	Normal Readings
Follicle-stimulating hormone	38–40 M.U.	48 M.U.	?	Over 40 M.U.	Cyclical: 15–20 M.U. 40–80 mid-cycle and menopause
Oestrogens ..	Nil (2 tests)	Less than 30 I.U.	?	"No excess"	15–50 I.U. Peak at mid-cycle 120 I.U.
17-ketosteroids (per 24 hours)	18·9 mg. (2 tests)	18·9 mg.	20·6 mg.	21·2 mg.	8–17 mg.
Pregnanediol	Trace: 3–4 mg.	Nil, only "pregnane" metabolite	?	Nil	Cyclical: 1–5 mg.

Gonadotrophins (Follicle-stimulating Hormone).—The readings (see table) cannot be correlated with the clinical condition of flushing, since they do not cover the period of severe symptoms. According to Nathanson *et al.* (1940) and Sharpey-Schafer (1940) a high level of excretion of anterior pituitary hormones might then have been expected. The final excretion level of over 50 M.U., however, was at the high level associated with the menopause.

Oestrogens.—At no time was evidence of excessive oestrogen secretion obtained either by complicated extraction from the urine or by direct injection of the natural urine.

17-Ketosteroids.—The normal limits of excretion vary from 8 to 17 mg. in 24 hours, and this level is generally exceeded in women with virilism not associated with an adrenal cortical tumour. There are, however, many cases of virilism on record with excretion levels within normal limits (Douglass, 1947).

Pregnanediol (Venning, 1938).—After hysterectomy a "pregnane" metabolite was present; its chemistry has not yet been elucidated. Miss Hain (1947) has extracted this substance on several other occasions, but its significance is not yet clear.

The Vaginal Smear as a Rough Mirror of Hormone Activity (McLaren, 1941).—Pre-operative smears and biopsy corresponded fairly well, the histology showing subacute vaginitis—that is, superficial mucosal desquamation with areas of subepithelial infiltration. Despite a prolonged search no cancer cells or cells resembling those seen in sections of the tumour were discovered. Fourteen months after operation her vaginal smear clearly reflected castration, containing mainly small basal and spinosum cells with many polymorphs.

Conclusions.—No unusual hormone excretion level was observed before or after operation. The level of gonadotrophin remained at the relatively high figure commonly found in menopausal women; the excretion of 17-ketosteroids (at between 18 and 21 mg. per 24 hours) probably reflected the hypertrophy which had been taking place in the remaining adrenal gland during the four years that had elapsed since unilateral adrenalectomy was performed.

Discussion

This case shows clearly the various phases of the vaguely defined endocrine illness which we have labelled adrenogenitalism. It is interesting that adrenalectomy led to improvement in the patient's acne vulgaris and to improvement in her general condition, although this may have been quite fortuitous after operation and rest in hospital. The enlarged adrenal (clinically assumed to be a tumour) and the follicular cyst probably represented only a phase of adrenogenitalism.

One is tempted to speculate on the reason why cancer of the uterus developed, although it may have been mere chance in a nulliparous woman approaching the climacteric. On the other hand, it seems certain that women suffering from adrenogenitalism are especially liable to develop tumours, not only in the pituitary but also in the adrenal, thymus, or ovary. Thompson and Eisenhardt (1943) have surveyed 98 cases from the literature with records of simple and malignant tumours in 76. Rare types of carcinoma have also been recorded. Crooke (1946) reviewed three cases of basophilism and recorded one of his own in which the pancreas (not Langerhans cells) was the site of carcinoma, while McLetchie and Scott (1942–4) reported carcinoma of an adrenocortical rest in the pancreas with bilateral adrenocortical hyperplasia and pronounced hypophysial abnormality.

The genital tract was involved in our case on three occasions: (1) amenorrhoea for a year, when the patient weighed 280 lb.; (2) six years later, when a follicular ovarian cyst was removed with her adrenal gland; (3) ten years later, when uterine bleeding led to a diagnosis of adeno-acanthoma of the uterus.

From the facts at our disposal we cannot say whether or not this patient's endocrine disturbances or the surgical removal of her adrenal gland had any bearing on the development of uterine cancer. Adrenalectomy seemed to have a temporary lowering effect on the excretion of 17-ketosteroids, but any operative procedure might do this. It is unlikely, moreover, that any temporary alteration of adrenal secretion after adrenalectomy would operate as a factor in the development of cancer three to four years later.

From the facts available, therefore, we must simply record the case as one of a fat, hirsute woman whose weight and blood pressure rose and fell over the years, and who at one stage developed carcinoma of the uterus with the

unusual features of adeno-acanthoma. Whether her ill-defined endocrine disturbances or surgical intervention had any bearing on the development of carcinoma is mere conjecture.

Summary

A case of adrenogenitalism is described in which over a period of 16 years surgery was necessary on three occasions: (1) to remove a hypertrophied adrenal gland; (2) to remove an egg-sized follicular cyst of the ovary; and (3) to remove the uterus for carcinoma (adeno-acanthoma). Hormone excretion levels were recorded before and after hysterectomy, but no unusual level was obtained.

I wish to thank Professor Hilda Lloyd, P.R.C.O.G., and Professor A. P. Thomson for the opportunity of reporting this case, and also Dr. A. M. Hain for the biological assays and help in their interpretations. Drs. W. St. C. Symmers and C. W. Taylor reported on the pathological sections, which were prepared and photographed by Miss M. E. Attwood.

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ERYSIPELOID OF ROSENBACH

EIGHT CASES TREATED WITH PENICILLIN

BY

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Erysipeloid, while not a common condition, occurs often enough for it to be borne in mind, particularly in any large clinic dealing with septic hands. Recently there have been several papers on this subject in this country (Hodgson, 1945; Singer, 1946; Barber, Nellen, and Zoob, 1946; King, 1946; Bush, 1949), and in America, Klauder (1938) records his experience on 100 cases which he has observed.

It is significant that, in spite of the increasing awareness of this entity, many cases must be missed or misdiagnosed, and the condition is not even mentioned in the second edition of Handfield Jones's *Surgery of the Hand*. I therefore wish to record eight cases occurring over the past 12 months (December, 1948, to December, 1949) among a total number of 385 septic hands seen at the clinic—that is, 2% of cases.

The responsible organism is *Erysipelothrix* (or *Bacillus*) *rhusiopathiae* (Browning and Mackie, 1949), which causes a disease in pigs known as "swine erysipelas." It is a Gram-positive bacillus, and human infection is mainly manifest by an erythematous lesion of the skin of the fingers, hand, or forearm. The bacillus is found among decomposing nitrogenous products. The condition is particularly prevalent amongst fishmongers, butchers, and housewives, who contract the infection by minor traumata to the fingers or hands while handling meat bones, poultry, or fish.

Case Reports

Case 1.—A man aged 32 punctured his left little finger while handling boxes of fish on December 12, 1948. He was seen by his own doctor on the 14th, when he complained of swelling of the finger. There was no constitutional upset. Injections of penicillin were given by his doctor twice daily, 200,000 units at a time, from December 17, when the condition appeared to settle, and he was allowed to use his hand from the 21st. The condition recurred on December 24, and his doctor then sent him to the casualty department as a "query bone infection of the finger." The little finger was swollen along its whole length, with a typical erythematous reaction of the skin. There was no heat in the part, the site of injury was healed, and there was no constitutional upset. The *x*-ray film of the finger was negative. He was given procaine penicillin, 300,000 units daily, from December 28 to January 5 inclusive, the hand being rested in a sling. On January 6 the condition had cleared, leaving a slight residual tenderness over the terminal interphalangeal joint.

Case 2.—A fishmonger aged 15 first attended the out-patient department on July 20, 1949. He had pricked his right index finger with a fish-bone on July 14, and had had intermittent inflammation since. On examination typical redness and swelling of the right index finger characteristic of erysipeloid were seen, and pronounced tenderness was present over the terminal interphalangeal joint. There was no lymphangitis, glandular enlargement, or constitutional upset. He was given 300,000 units of procaine penicillin daily by intramuscular injection for five days, when the condition rapidly subsided.

Case 3.—A butcher aged 20 first attended the casualty department on September 28, 1949, with a "septic" left middle finger, sustained from a scratch from a bone eight days previously. The day after injury the finger felt sore, but it improved until September 27, when it became inflamed. On examination of the middle finger of the left hand there was the typical erysipeloid reaction, localized particularly over the proximal interphalangeal joint. There was no fluctuation, lymphangitis, or lymphadenitis. He was given 300,000 units of procaine penicillin daily, antiphlogistine was applied to the finger, and the hand was rested in a sling. Penicillin was discontinued on October 1, and the patient was discharged on the 3rd. He returned the next day with a recurrence of the erysipeloid on the third finger, but this time spreading also to the fourth finger over the dorsum of the hand. After a further course of penicillin for five days the condition cleared completely.

Case 4.—A butcher aged 21 first attended hospital on October 5, 1949, having scratched his right hand with a meat bone in the region of the dorsum of the metacarpo-phalangeal joint of the little finger on September 26. He had swelling and pain in the hand, with the usual erysipeloid reaction. He was given 500,000 units of procaine penicillin immediately, and continued with 300,000 units daily for five days. He was then discharged cured.

Case 5.—A housewife aged 36 first attended hospital on October 5, 1949. She had scratched the third finger of her left hand on September 30 while cutting up fish. There was an erythematous infiltration of the finger. The customary dosage of 300,000 units of procaine penicillin was given daily up to and including October 12. The patient was discharged cured on October 13.

Case 6.—A fishmonger aged 38 attended hospital on October 16, 1949, having injured the dorsum of the proximal interphalangeal joint of his left ring-finger on October 9 while cleaning out ice from a fish box. The typical erythematous appearance of the skin was present. Procaine penicillin, 300,000 units daily, and local antiphlogistine were given. He was discharged on October 27 with the condition healed. There was a scaly desquamation of the skin, and full movements of all the finger-joints were present.

Case 7.—A fishmonger aged 22 attended hospital on November 1, 1949, with a swollen and reddened left forefinger. He could not bend the finger. There was no constitutional upset, enlarged glands, or lymphangitis. A week previously he had pricked his finger on the volar aspect of the base of the second phalanx. The finger swelled several days afterwards and was painful and red. After poulticing, the swelling subsided, but it recurred again and 300,000 units of procaine penicillin were given daily for seven days. The condition cleared, leaving no residual effects.

Case 8.—A fishmonger aged 35 first attended hospital on November 5, 1949, with a swelling of the right forefinger. There was some axillary adenitis. On October 31 his forefinger was painful and seemed "inflamed" (red) on the dorsum of the distal phalanx. There was no noticeable skin trauma. The next day there was some improvement, which continued until November 4, when the right forefinger became very painful, red, and swollen in appearance. He had kept at his work all this time. The usual course of 300,000 units of procaine penicillin with local antiphlogistine was given for five days, when the condition completely cleared.

Comment

Three well-defined clinical categories of *Erysipelothrix rhusiopathiae* infection in human beings have been described: (1) the localized cutaneous form (erysipeloid of Rosenbach); (2) a severe generalized cutaneous form; and (3) a septicaemic form with or without cutaneous involvement (Klauder, 1944).

Bacteriological proof of the infection can be established by "the microscopical demonstration of the organism in the lesions or blood and its cultivation from these sources" (Browning and Mackie, 1949).

In view of the ease in diagnosing the condition clinically, biopsy of the lesion is not justifiable. Herman (1946) rightly pointed out that the condition may be mistaken for a septic arthritis, for the maximum tenderness seems to centre around the interphalangeal joints. This tenderness in the region of the joints has also been commented upon by King (1946). Another characteristic of this condition is the spread of the erythema up one finger across the web, usually on the dorsal aspect of the hand, and then down the adjacent finger (Dolton, 1946).

Constitutional upset is very seldom seen and was not present in any of the eight cases recorded here, although glandular enlargement may occur and sometimes a mild lymphangitis. Sequeira, Ingram, and Brain (1947) attribute constitutional upset and the occurrence of lymphatic-node involvement and lymphangitis to any secondary infection which may accompany the initial inoculation with the *Erysipelothrix rhusiopathiae*. This fact would appear to be borne out by the first of the five bacteriologically confirmed cases described by Barber *et al.* (1946). Here the "response of the lymphangitis to sulphamezathine (sulphadimidine) suggested that some other organisms were responsible, as the erysipeloid itself was so strikingly unaffected by the sulphamezathine."

Suppuration nevers occurs, no matter how long the case may go without treatment. This important point should be borne in mind, for many an unwary house-officer may be tempted to incise the lesion at its most painful spot without any benefit accruing.

Erysipeloid is a self-limiting disease, and varying periods have been given for the length of time it may run its course before fading out if no treatment is given: seven days to eight months by Klauder (1938), and one to six weeks by Sequeira *et al.* (1947); and Stiles (1947) records a case of chronic erysipeloid of nine years' duration which was eventually cured by penicillin.

Cases 1 and 3 relapsed after an inadequate period of treatment. This feature of relapse and recurrence of the erysipeloid has been stressed by all writers on the subject, and confirms that no immunity is conferred by the first attack of the condition.

A notable feature was that six out of the eight cases were seen within five weeks, from September 28 to November 5, 1949. King (1946) has suggested a seasonal incidence for erysipeloid, with a predominance of the condition in the autumn, when swine erysipelas is more prevalent in England, and flies may be a vector of the disease. The time of occurrence of the cases here recorded would tend to substantiate his claim.

Treatment

Treatment is essentially medical and penicillin is without doubt the choice. The sulphonamides are ineffective against this condition (Klauder and Rule, 1944), and serum therapy is not certain and is open to the objection that the patient is very liable to serum sickness. The earliest reports of penicillin treatment in human infection with erysipelothrix are those of Hodgson (1945) and Barber *et al.* (1946). I have found that 300,000 units of procaine penicillin given daily by intramuscular injection for at least five days will cure the lesion.

It must be stressed that for penicillin to be effective treatment must be adequate and prolonged. This conclusion was also reached by Bush (1949), Lowden (1949), and Erskine (1949). Local treatment may be given in the form of antiphlogistine and resting the arm in a sling.

I wish to thank Dr. J. M. Greenwood, medical superintendent Withington Hospital, for permission to publish these cases.

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CORACOCLAVICULAR JOINT

A RARE CONDITION TREATED SUCCESSFULLY BY OPERATION

BY

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Anomalous joints between the clavicle and coracoid processes are occasionally reported as anatomical or radiological curiosities, and I have been able to trace 54 in the world literature, including one in this country. Of these 49 are non-surgical cases, noted on skiagrams or at necropsy, three are recorded by Myer (1915–16), and two have required operation for relief of severe pain developing at the age of 34. The case recorded below has a similar age incidence, at 38.

Case Report

This patient, a talented organist aged 40, had undertaken fairly long hours of clerical work in recent years. He first developed symptoms two years ago, the earliest sign being faint "pins-and-needles" in the fingers of the right hand and later the type of numb feeling associated with pressure of the arm over the back of a chair. At first the attacks were spaced several weeks apart. Later an ache developed in the middle of the extensor surface of the forearm and later still in the middle of

the flexor aspect. Another symptom, which still persists slightly, was the loss of power of full and rapid pronation and supination required for playing fast and elaborate piano pieces. Analgesics gave little relief, but some improvement occurred after large doses of vitamin B_1 by mouth. A complete remission occurred from January to July, 1948, only to be followed by almost continuous pain in the forearm, worse on the ulnar side. In addition his head began to be pulled downwards and forwards, and lifting the chin or pulling it back caused pain in the right axilla. Pain was lessened by exercise and made worse by rest.

Examination.—Except for some limitation of abduction, physical signs were entirely absent. No tenderness could be elicited along the clavicle, nor could any abnormality be felt, even when the abnormal joint had been demonstrated by skiagrams (Fig. 1). These, taken in September, 1948, showed the

FIG. 1.—Before operation. Showing normal left clavicle and abnormal right clavicle.

FIG. 2.—Before operation. Showing the abnormality of the right clavicle in greater detail.

anomalous articulation on the right side about the junction of the outer and middle thirds of the clavicle, the left side being completely normal (Fig. 2). In view of the rapidly increasing disability, operation was advised. At that time I had not been able to trace any comparable case in the literature, so that a special approach had to be devised. Stereoscopic radiographs showed the clavicular exostosis to be infero-posterior to the clavicle, and, as already noted, it could not be palpated externally. A fellow surgeon whom I consulted advised temporary dislocation of the acromio-clavicular joint to ensure the safety of the underlying brachial plexus and subclavian vessels; but this, involving the division of the deltoid muscle as well, seemed too destructive a technique for a patient of such marked artistic abilities. Although his neck was large and his shoulder massive, it was thought that sufficient access might be obtained through the clavicular part of the pectoralis major, and this route was eventually chosen.

Operation.—Under general anaesthesia, with the head rotated away from the affected side, a linear incision was made along the middle third of the clavicle, later extended towards the acromion process. After a careful dissection underneath the clavicle the abnormal joint was found to be further out than was expected, and only a narrow triangle could be obtained for operative access. The soft tissues, including fibres of the pectoralis minor muscle, were cleared from the anterior surface of the exostosis by blunt dissection. With the index finger of the left hand behind the abnormal joint to guard against accidental damage to the deeper tissues, an osteotome was applied to the base of the clavicular outgrowth and given gradually harder hammer blows by my assistant till a clean split was obtained. It was just, and only just, possible to obtain the necessary angulation for the osteotome. After about a dozen taps the separated piece of abnormal bone was twisted out with lion forceps. The under surface was seen to be well lined with articular cartilage. The coracoid process, lying deeply in a deposit of fat and connective tissue, was left alone and the operation was completed by suture in layers.

Progress.—Convalescence was uneventful except for some serous discharge from the inner end of the wound, probably due to too liberal a dusting with penicillin and sulphathiazole powder. Movements of the arm and hand were encouraged from the start, and no restrictive bandages were placed on the shoulder. The patient was allowed up from the day of operation, and found himself free from the original pain when he recovered from the anaesthetic. Ten days later he was playing brilliant passages on the ward piano, and a few days afterwards he was able to play complete oratorios on various church organs. Fig. 3 shows the condition after operation. Eighteen

FIG. 3.—Right clavicle after operation.

months after operation he is free from pain, but still finds slight limitation of rapid twisting movements of the right forearm. He also says, quite unaccountably, that his pedal work is not as good as before.

Discussion

Two previous surgical cases are recorded, the last by Dr. Gustavo Wertheimer (1948), of Brazil, who also describes a similar case treated by del Valle and Giordano (1943), in the Argentine. The first was that of a male negro of 37 with a three-year history of shoulder-joint pain, later radiating to the left arm, persisting during rest, and increasing with exercise. The second patient, a white woman of 35, had pain in her left shoulder for one year, radiating to the breast, neck, and left arm. The pain became steadily worse and was not relieved by analgesics. The maximum intensity persisted at the site of the abnormal joint. Occasional symptoms included itching of the last four fingers, followed by transient paralysis of the hand. Both cases obtained complete relief from operation, which consisted of excision of the anomalous joint by osteotomy through the deltoid muscle after wide exposure of the pectoralis minor and coracobrachialis. Most of the other cases have been symptom-free throughout, but Frasseto (1921) records a bilateral case in which fracture of the surgical necks of both humeri recurred in two falls, the abnormal fixation of the clavicle no doubt being a contributory factor.

Arthritis in one of these joints has been described by Timpano (1934) in a workman of 63.

It is interesting to note that the three surgical cases were symptom-free until their ages reached 38, 34, and 34 respectively, and that the pain became rapidly worse and intolerable, being completely relieved by removal of the joint or the clavicular outgrowth. The aetiology of the pain is most obscure. Del Valle and Giordano (1943) ascribe it to a sympathetic or plexal origin due to compression of microscopic nerves, which are relieved by removal of the anomalous joint. Arthritic changes and joint degeneration are considered to be causal factors, and the joint is certainly in very close proximity to the main trunks of the brachial plexus, although it is difficult to see how these could be affected by pressure from a closed joint.

Lastly, a practical point. The skiagram was misleading, and it was not realized that the clavicular outgrowth actually articulated with the coracoid process until it was found that lifting the arm above the shoulder gave no improvement in operative access. Shortly afterwards, of course, an actual joint, lined with articular cartilage, was demonstrated.

I am very grateful to my colleagues, Mr. C. S. Milne and Dr. T. J. Shields, for their invaluable help in exploring the literature of this case.

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Medical Memoranda

Recovery from a Ruptured Mycotic Aneurysm

In reporting this case we recognize the fact that a diagnosis of subacute bacterial endocarditis was not established beyond dispute by a positive blood culture. However, we think that readers will be in little doubt about the nature of the underlying pathology, and if our diagnosis is accepted on clinical grounds this case would seem to be unique. We have read of one similar case surviving the rupture for two and a half weeks only.

CASE REPORT

A girl aged 15 was brought to the out-patient department by her mother on November 4, 1948, with the history that she had been losing weight, colour, and energy ever since a tonsillectomy in the preceding January. According to her mother she had "gone an awful colour" and would not leave the house or show interest in anything. She had been having pains in her knees and ankle-joints, and a sharp intermittent substernal pain, both on exertion and at rest. She denied having chilly feelings, sweats, painful nodes on her fingers, etc. Her previous illnesses consisted of scarlet fever followed by rheumatic fever at the age of 9, further attacks of rheumatic fever at 12 and 13, and acute rheumatism at Christmas, 1947. During none of these attacks had she suffered in health to the extent that she had recently.

On examination she was seen to be a tall thin girl, with a café-au-lait discoloration of the skin. Her pulse rate was 120 and regular, and her blood pressure 125/75. The apex beat was displaced slightly to the left and auscultation revealed a well-marked mitral regurgitant murmur. There were no signs of congestion of the lung bases or liver, and no oedema. The spleen was not palpable, and her fundi oculorum showed no abnormal changes, but there were fairly numerous petechial haemorrhages on the trunk, especially on the flanks. Both knee-joints were tender and contained fluid. She was admitted to hospital on November 10.

Special Investigation.—A blood count showed: haemoglobin 75%; red cells, 4,700,000; colour index, 0.8; white cells, 9,000 (polymorphs 85%, lymphocytes 11%, monocytes 4%). E.S.R., 40 mm. (Wintrobe). Urine: no red blood cells or other abnormalities were found in the centrifuged deposit on repeated occasions. Blood culture on three consecutive days was sterile after 48 hours. A radiograph of the chest revealed nothing abnormal. It was decided to start treatment with penicillin without delaying any further in the hope of obtaining a positive blood culture, and 250,000 units were given six-hourly for 50 days.

On admission and for 48 hours after starting the penicillin her temperature was remittent between 101 and 99° F. (38.3 and 37.2° C.). Her pulse during this period varied between 110 and 130. From then onwards until December 5 her temperature rose only to 99° F. or less in the evenings and her pulse was 110. During the early hours of December 4 she awoke with a severe headache, vomited, and later became unconscious. There were a left-sided hemiparesis at the onset and neck rigidity. The depth of unconsciousness gradually deepened.

Lumbar puncture showed a pressure of 245 mm. and a heavily blood-stained fluid. During the next few days head retraction was most pronounced. Haemorrhages appeared around the optic disks.

Her temperature was considerably elevated during this phase of her illness, but had settled to about normal by December 11, and rose only on occasion after this.

Recovery was gradual. By December 14 she had regained normal clarity of consciousness, but there was still marked neck rigidity. By December 17 the C.S.F. was reported as being xanthochromic and containing 200 cells per c.mm.—50% red blood cells, 50% lymphocytes.

On December 30 she sat in a chair for the first time, and was discharged home to a convalescent regime on January 4, 1949. At this time her weight was 7 st. 8 lb. (48 kg.), haemoglobin 90%, and E.S.R. 14 mm. (Wintrobe).

She has attended the out-patient department regularly since discharge. On her last visit (July 5) she looked in perfect health, was leading a normal life, and was helping her parents in their business. Her weight was 8 st. 10 lb. (55.3 kg.), haemoglobin 94%, and E.S.R. 8 mm. (Wintrobe). The only abnormal physical sign was her mitral murmur.

Her last attendance was on December 6, 1949, when she was free of symptoms and her weight was 9 st. 3½ lb.

COMMENT

The discursive element of this case revolves around the diagnosis. This girl had a subarachnoid haemorrhage either from a mycotic aneurysm or from a congenital (Berry) aneurysm. In the former case her serious decline in health, the petechial haemorrhages, and the valvular lesion can be satisfactorily correlated. In the latter, these significant facts must be attributed to the rheumatic process complicated by a second pathological process. We consider the former diagnosis much the more probable.

Numerous reports have appeared in the medical press concerning the results of treatment of bacterial endocarditis with penicillin. Paul, Bland, and White (1947) report the case of a man who succumbed to congestive cardiac failure two and a half weeks after a subarachnoid haemorrhage. At necropsy, in addition to subarachnoid and intracerebral haemorrhage, it was found that rupture of a chorda tendinea of one leaf of the mitral valve had taken place. These authors report the case of another patient who died from subarachnoid haemorrhage at the end of a course of treatment. Cultures of the involved valve and the blood were negative.

The tendency in treatment is towards a higher dosage of penicillin. Our case received a million units daily for 50 days.

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Skin Eruption in Newborn due to Bromism Derived from Mother's Milk

French states that "bromide and iodide eruptions have been recorded in infants at the breast when the mother has been taking the drug without presenting any cutaneous symptoms herself." In the following case the main point of interest is that the rash did not appear until 11 days after the mother had stopped taking the drug.

CASE REPORT

The patient was the third premature child of a mother who had had antenatal toxaemia during all her three pregnancies. She had had adequate antenatal care and a diet with a high vitamin content, and her general health had been normal before the appearance of the toxaemic symptoms. The Kahn test was negative. The expected date of confinement was March 27, 1949. On January 25, at about the 32nd week of pregnancy, she complained of headache and slight general oedema. Her blood pressure, which was 120/80 mm. Hg on January 4, rose to 165/105, and there was a trace of albumin in her urine.

On admission to hospital on January 26 she was kept in bed and put on a salt-free diet. Potassium bromide and chloral hydrate, each 20 gr. (1.3 g.), were given twice daily. Her symptoms began to abate and the daily urinary output was adequate. The resting blood urea on February 4 was 30 mg. per 100 ml. From February 2 potassium bromide and chloral, same dosage, was given only once every night, although the salt-free diet was continued. On February 11 she went into premature labour, resulting in the spontaneous delivery of a male baby, premature and rather blue. The mother appeared quite well after delivery, although her blood pressure was raised to 160/118. The last dose of potassium bromide and chloral was given that night. The blood pressure dropped to 126/94 the next day and urination was adequate. Normal diet was resumed on February 14. No cutaneous lesion appeared in the mother.

The baby's birth weight was 3 lb. 8 oz. (1.59 kg.). The usual treatment for premature babies was carried out. Half-strength normal saline was at first given and later quarter-strength expressed breast milk was added. When the mother's lactation was established all her milk was given to the baby. On the eighth day the baby received full-strength expressed breast milk, 2 fl. dr. (7 ml.) hourly, with the addition of half-strength saline. On the tenth day its body weight was 3 lb. 10¼ oz. (1.65 kg.).

On February 21, 10 days after birth, two white spots were noticed on the baby's gums. These disappeared after painting with 1% gentian violet solution.

On February 22 discrete vesicles 1–2 mm. in diameter appeared on the forehead. Their base was pinkish and the content was clear. They were painted with gentian violet. Next day they became pustules, and more were noticed on the cheeks, chin, neck, and chest, with a few on the back, abdomen, and extremities. There was no sign of systemic disturbance or of irritation. Penicillin was given intramuscularly in doses of 5,000 units four-hourly. On February 24 more vesicles and pustules appeared. The child's general condition was the same. Penicillin was increased to 10,000 units four-hourly. No growth was obtained from the aspirated pus. The accompanying photograph was taken on February 27.

By February 28 pustules were present all over the body. The new ones were discrete, of pin-head size, with redness around the base. The older ones increased in size and became confluent, forming pustules about 3–5 mm. in diameter. The biggest and most abundant were on the forehead. They spread from the cheeks to the eyelids. Lower down the body they were more discrete and fewer in number. There were one or two on the scrotum and on the palms and soles. These had no red base. There was still no sign of irritation and the baby seemed to be extraordinarily comfortable and quiet. His body temperature was normal and his weight had increased to 3 lb. 13 oz. (1.73 kg.). Penicillin seemed to have no effect at all on the rash.

One of the consultants, Dr. G. V. A. Griffiths, suggested that it might be a bromide rash derived from the mother's milk. On February 26 a sample of the mother's milk was sent for analysis, and approximately 120 mg. of bromine per 100 ml. of milk was found. The mother's milk was therefore withheld, condensed milk being given instead. From then onwards no fresh eruption appeared, and those present began to dry up. The baby started to cry more. By March 7 all the rash had dried up, and the lower parts of the face and the rest of the body were cleared. On March 9 he weighed 4 lb. 4½ oz. (1.94 kg.) and on March 11 mother and child were discharged from hospital, their condition being completely satisfactory.

Photograph taken six days after the eruption began.

Analysis of the mother's milk and urine on March 2 showed: milk, chloral absent; urine bromides equivalent to 6.3 mg. of bromine per 100 ml. On March 7 no significant quantity of bromides was present in the specimens submitted.

COMMENT

There is no doubt that the baby's skin eruption was due to bromide derived from the mother's milk, as the withholding of the latter resulted in rapid recovery. It is interesting to note the following points: (1) The rash did not appear until 11 days after delivery, although bromides were given to the mother before but not after delivery; this suggests that the drug was not passed to the foetus *in utero* but mainly through the milk. (2) Added salt in the baby's diet, in the form of half-strength saline, although very small in amount, did not prevent the accumulation of bromides. (3) The mother had no cutaneous manifestation. (4) Bromides were excreted in greater concentration in the milk than in the urine. (5) It took over 20 days for the mother to get rid of it all, although a salt-free diet was no longer given. The kidneys could not of course be regarded as 100% efficient.

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A circular from the Ministry of Health states that some accounts in the Post Office Savings Bank have been opened on behalf of certified mental defectives who are incapable of understanding how to operate the accounts. Accounts of this kind should be opened only when the patient fully understands the nature of the transactions involved.

Reviews

PATHOLOGY OF NEUROSURGERY

Neurosurgical Pathology. By I. Mark Scheinker, M.D. (Pp. 370; 238 figures. 45s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1949.

Neurosurgery has developed to a stage at which it might well be considered to need a pathological textbook. It should be made perfectly clear therefore that the present work is nothing of the sort; it is better described as a compilation of three short monographs entitled cerebral swelling, nervous system injuries, and tumours of the nervous system. Two short chapters follow, on cerebral abscess and hydrocephalus, but the treatment of neither of these subjects is profound.

The overwhelming importance of cerebral oedema needs no emphasis; it is often unpredictable and inexplicable. The author traces the condition of "cerebral swelling" through three stages, designated as tumefaction, oedema, and liquefaction. The first appears to be the equivalent of the German concept of "Hirnschwellung," a condition in which it is postulated that the brain volume increases without hyperaemia or excess of free fluid. This, according to the author, is due to a circulatory disturbance producing swelling of the nerve fibres, but how or why it occurs remains a mystery.

Injuries of the central nervous system are not comprehensively treated, but there is a deliberate selection of the little-understood generalized and remote sequelae of injury at the expense of the more obvious and explicable effects produced at the site of trauma. These earlier sections, treating of difficult aspects of neuropathology, are of greater value than the chapter on intracranial tumours. Here it is regrettable that the author should encourage the view (p. 147) that the haematoxylin and eosin stain is adequate for the diagnosis of almost all types of tumour. Even the expert would be sadly at a loss if restricted in this way. The description of tumour types is, for the most part, unmodified from Bailey and Cushing. It is little influenced by more recent work, except for three dubious additions—the subependymoma, the infundibuloma, and diffuse cerebral glioblastosis. The polar spongioblastoma is omitted, however. Incidentally, why is it that F. B. Mallory's classical account of the ependymal gliomas, published in 1902, has been so consistently ignored in recent decades? Exception may be taken (p. 168) to the suggestion that diagnostic irradiation of the medulloblastoma should be undertaken without histological verification; this policy has surely been outdated by the mistakes that have followed its use. In brief, this is a provocative book, perhaps better suited to the clinician than to the neuropathologist. Its illustrations are both excellent and numerous.

DOROTHY S. RUSSELL.

COMMON FEVERS

The Common Infectious Diseases. By H. Stanley Banks, F.R.C.P., D.P.H. (Pp. 354; illustrated. £1 1s.) London: Edward Arnold. 1949.

More new textbooks on infectious diseases have been published in recent years than in the preceding forty, which is natural enough when one considers the changed outlook resulting from the introduction of chemotherapy. This new British contribution is worthy to rank among the best. The author has managed to compress into some 350 pages a sound and balanced account of the infectious diseases commonly seen in this country, with adequate emphasis on the correct principles.

As one would expect, Dr. Banks's description of the meningococcal infections is full and well documented. His own cases are analysed to show the fundamental points, and although the chapter may contain nothing new to those who are familiar with this group of infections and with the author's contribution to their study, the novice will obtain here a first-class account of the essential unity of "meningococcal fever." One small point might be made in connexion with treatment—there may be a place for a single intrathecal injection of penicillin at the first lumbar puncture. At the present time, when the other acute forms of meningitis are as common as the meningococcal type, there is advantage in giving the patient the widest possible protection: at the first lumbar puncture it is seldom possible to be dogmatic about the nature of the infective organism. With his main contention, that sulphonamides are the best therapy for meningococcal infections, there can be no disagreement.

In the chapter on pertussis adequate (and overdue) emphasis is given to atelectasis, and a series of well-reproduced radiographs depict the common appearances of collapse in different parts of the lung. This is, I think, the first textbook of infectious diseases adequately to discuss this important aspect of the one condition which still holds some terror. The black-and-white reproductions of photographs of rashes are, as so often the case, somewhat disappointing. It is unfortunate that coloured illustrations are still an expensive luxury, for the half-tone plate is a poor substitute.

The student—graduate or undergraduate—has now a wide choice of British and American textbooks on infectious diseases. Some of these are rather pretentious and fail as practical manuals, because the attempt to include everything results in a lack of balance; others show little appreciation of the change in outlook which the recent advances in therapy have induced, and as a result are woolly and diffuse. This present volume avoids such criticism. Its excellence lies in the obvious good judgment that its author has shown in emphasis. It is of a size and compass to form the ideal student's textbook, and the general practitioner will not only find it interesting at his first reading but will want to keep it among his common reference books. It is undoubtedly first class.

T. ANDERSON.

A THYROID REVOLUTION?

The Thyroid Hormones and their Action. By G. Mansfeld, M.D. Translated by E. Pulay, M.D. (Pp. 157. £1 4s.) London: Frederick Muller. 1949.

For most Englishmen, to read this book is to embark on fresh seas charted by strangers whose cartographical skill they have no means of estimating. One is asked to accept, on the authority of workers whose very names are strange to one's ears, a series of conclusions so wide in their significance, of such great practical importance, and at the same time of such staggering heterodoxy, that at a first reading one may be forgiven for wondering whether one is being admitted to the privileged first view of the garden of a master of horticulture or just being led down the garden path.

Reviewers are generally believed to glance rapidly through the books submitted to them and then to write of them

in a style in part dependent upon whether the authors belong to the same club. It is therefore important to say that I am now reading Professor Mansfeld's book for the third time. The first time I was so acutely conscious of our belonging to different clubs that until I neared the end I was inclined to return it, accompanied by the simple statement that I could not understand it. But something towards the end suddenly enlightened a dark corner in my mind. I read it a second time with understanding and enjoyment. Perhaps I shall see through it the third time, but till then I am bound to say that no one whose interest lies in thyroid disorders can afford to neglect it.

We have been accustomed to believe that the healthy thyroid gland produces but one hormone, of which the active part is thyroxine. Mansfeld would have us believe that there are four: one which is concerned with blood formation, which he calls the myelotropic hormone; two which have the effect of lowering oxygen consumption, one of which comes automatically into action in the spring and one when the body is overheated—these he calls the thermothyrins; and one which we are unashamedly relieved to find is our old friend thyroxine. His statements are supported by many well-controlled experiments which command respect, and are of the greater importance now that pure thyroxine is coming into clinical use. They suggest that we shall not find that thyroxine is capable of replacing thyroid in all respects.

Indeed, our relief at finding thyroxine among the thyroid hormones may have been premature. It is not the simple stuff we thought it was. It is apparently true that it raises oxygen consumption by its action on the cells themselves and not, as some have tried to persuade us, by an action on the central nervous system. But the nerves are none the less necessary, for they are the channels along which thyroxine slowly reaches the cells. It has, moreover, other effects. By acting on the pituitary it causes the production of a hitherto unknown hormone which travels by the blood stream and immediately raises the oxygen consumption of resting muscles. A third activity is even more complicated. In its absence the thermothyrin B reverses its normal effect and raises oxygen consumption, whereas another substance in colloid is necessary for the normal activity of thermothyrin A, thyroxine actually increasing its metabolic effect in thyroidectomized animals.

The last chapter, on Graves's disease, might well have been omitted. It is full of stimulating speculation, but it lacks the solid, or seeming-solid, basis of experiment which gives the earlier chapters their value.

RAYMOND GREENE.

MEDICAL PROTOZOOLOGY

Handbook of Medical Protozoology. By Cecil A. Hoare, D.Sc.(Lond.) (Pp. 334; 43 figures. £1 15s.) London: Baillière, Tindall and Cox. 1949.

This new handbook on medical protozoology fills a gap in the literature available to the student of this subject. The early chapters on the structure, physiology, classification, and ecology of the protozoa give the reader an excellent introduction to the group to serve as a foundation for subsequent more detailed study. There follows a consideration of the intestinal protozoa of man in which clear descriptions are given of the four groups which occur in the intestinal tract—the amoebae, the flagellates, the coccidia, and the ciliates—and there is a separate chapter on the coprozoic protozoa.

One of the best sections of the book is that on the haemo-flagellates, the leishmanias and trypanosomes. A good description of the former includes not only morphological details of the parasites in the vertebrate and insect hosts but considers their classification, cultivation, transmission, and host-parasite relationships. In describing the trypanosomes the author is in his own specialty and threads a skilful way through the intricacies of classification and differentiation of species, which is summarized in a key to the important mammalian trypanosomes.

The morphology, life-cycles, and methods of transmission of the important species are discussed individually, the fullest account naturally being that relating to the African pathogenic species and their vectors the tsetse flies. Somewhat surprisingly, considering their importance, the malaria parasites are the last big group to be discussed. The description of these follows orthodox lines and there is nothing left out which the student should know. This statement emphasizes sufficiently the value of this section.

The third part of the book describes the methods of collecting materials for study, the making of permanent preparations, methods of diagnosis, and media for cultivation of various protozoa. The three coloured plates are excellent and the general format of the work very pleasing. It can be recommended as the most useful introductory work on medical protozoology for the student and medical officers and practitioners in the Tropics.

H. E. SHORTT.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Fifty Years in Midwifery. The Story of Annie McCall, M.D. By P. Barrass. (Pp. 121. 6s.) London: Health for All Publishing Company. 1950.

Lectures on Medicine to Nurses. By A. E. Clark-Kennedy, M.D., F.R.C.P. Foreword by C. Alexander (Pp. 288. 15s. 6d.) Edinburgh: E. and S. Livingstone. 1950.

The Production of Antibodies. By F. M. Burnet, M.D., F.R.S., and F. Fenner, M.D. 2nd ed. (Pp. 142. 12s. 6d.) London and Melbourne: Macmillan. 1949.

Stern's Applied Dietetics. Revised by H. Rosenthal, B.S., P. C. Baker, B.S., and W. A. McVey, M.D. 3rd ed. (Pp. 293. 38s. 6d.) London: Baillière, Tindall and Cox. 1949.

L'Acupuncture du Praticien. By H. Voisin. (Pp. 192. 420 francs.) Paris: Librairie Maloine. 1950.

Les Veines. By J. Louvel and J.-J. Laubry. Preface by Ch. Laubry. (Pp. 220. 460 francs.) Paris: Librairie Maloine. 1950.

Traité de Médecine. Vol. 10. Maladies du Cœur. (Pp. 1,167. 3,600 francs.) Paris: Masson. 1948.

Traite de Médecine. Vol. 12. Maladies du Sang et des Organes Hématopoiétiques. (Pp. 727 2,400 francs.) Paris: Masson. 1949.

Traité de Médecine. Vol. 14. Maladies des Reins. (Pp. 920. 2,800 francs.) Paris: Masson. 1949.

Traité de Médecine. Vol. 15. Maladies du Système Nerveux. (Pp. 1,254. 3,400 francs.) Paris: Masson. 1949.

Traité de Médecine. Vol. 16. Maladies du Système Nerveux. (Pp. 1,251. 3,400 francs.) Paris: Masson. 1949.

Die Entwicklung der Lungentuberkulose im Röntgenbild. By E. Zdansky. (Pp. 67. 20s. 6d.) Vienna: Springer. 1949.

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INFECTIOUS MONONUCLEOSIS

Interest in glandular fever in this country was aroused by Tidy's[1] work shortly after the first world war, though Dawson Williams[2] had given an account of the disease in 1897. It is evident from a scrutiny of the literature that has appeared during the last thirty years that the disease is now more common than it used to be, that in epidemics the same age groups are not invariably affected, and that the pathological changes are more widespread throughout the body than is often realized. It is difficult to estimate the incidence of a disease which is not notifiable and which, as Mitchell and Zetzel[3] point out, can resemble other diseases so closely. In 1921 Tidy[4] stated that during eighteen months' experience in a fever hospital he could not remember seeing a case. Infectious mononucleosis is still considered one of the less common infections, but most medical officers in fever hospitals will encounter at least half a dozen cases in a similar period to-day. Gardner and Paul[5] record that in the period 1923–9 admissions to their glandular-fever unit were on an average only four a year, whereas 20 cases were diagnosed in 1945. No doubt some of this increase can be attributed to the greater use of the Paul–Bunnell test to confirm the diagnosis, but this can hardly be the whole explanation.

Cases of infectious mononucleosis are usually sporadic, but extensive epidemics can occur. In 1930 there is little doubt that the infection was widespread over the South of England,[6] and more recently Halcrow and his colleagues[7] have described what must be regarded as a large outbreak in Stirlingshire during 1942: a valuable feature of their account was the disclosure that latent infection was common in the district surrounding the hospital. Latent infection would, of course, explain the apparent infrequency—in ordinary familial experience—of frank case-to-case infection, and it seems probable that manifest cases form a small proportion of the total number infected. In contrast to the usual low communicability in household infection Tidy and Daniel[8] and many others have drawn attention to the high attack rate in outbreaks in closed communities such as residential schools. Although its epidemic behaviour is thus far from clear, it is fairly certain that infectious mononucleosis is now always, or nearly always, present in urban areas; it may frequently be diagnosed as atypical scarlet fever, measles, or rubella, but, unlike them, it often causes long periods of disability. Isaacs[9] has drawn attention to the chronic course of the illness in some patients, and found that the administration of suprarenal cortical extract gave good results.

Consideration of the age distribution also discloses gaps in our knowledge of the disease. Tidy and Morley[4] stated in 1921 that 80% of the cases occurred in children under 12 years of age. In the English epidemic of 1930, however, adults were more often infected than children[6]; this is more in keeping with Bernstein's[10] experience, 81% of whose patients were between 15 and 30 years of age. More recently Gardner and Paul[5] reported a series in which 51% of the patients were between 21 and 30 years. Evaluation of many of the wartime reports is difficult, because the writers' cases were drawn from a selected Service population. Tidy[11] has suggested a possible explanation for the difference in the age distribution in Britain and the U.S.A.: reported outbreaks in the latter were mainly among students, whereas in Britain they were mainly among boys at preparatory and boarding schools. No doubt difficulty of diagnosis is also partly responsible for the apparent greater frequency of the disease in adults: it is more natural to question a diagnosis of measles or scarlet fever in an adult of 25 than in a child of 5 or 6. Typical and, indeed, severe infections are of course seen in young children, but, as with acute hepatitis, it may be that pathological changes are more frequently minimal when the infection occurs during early life, so that the disease is less apparent. Infectious mononucleosis resembles anterior poliomyelitis in that the suspicion has arisen that a disease originally regarded as sporadic has acquired epidemicity, as well as a tendency to attack an older age group.

Swelling of the glands is merely the obvious sign of a more generalized systemic reaction. Although most clinicians no doubt realize this when confronted with a patient suffering from a severe infection, in milder cases it is easy to be misled into considering the disease as

1 *British Medical Journal*, 1921, **1**, 100.
2 *Lancet*, 1897, **1**, 160.
3 *War Med.*, 1944, **5**, 356.
4 Tidy, H. L., and Morley, E. B., *British Medical Journal*, 1921, **1**, 452.
5 *Yale J. Biol. Med.*, 1947, **19**, 839.
6 Tidy, H. L., *Proc. R. Soc. Med.*, 1931, **25**, 155.
7 *British Medical Journal*, 1943, **2**, 443.
8 *Lancet*, 1923, **2**, 9.
9 *Blood*, 1948, **3**, 858.
10 *Medicine, Baltimore*, 1940, **19**, 85.
11 *Blood*, 1948, **3**, 823.
12 *Amer. J. Path.*, 1947, **23**, 463.
13 *Blood*, 1948, **3**, 830.
14 *Lancet*, 1946, **2**, 753.
15 Ibid., 1946, **2**, 819.
16 *Blood*, 1947, **2**, 217.
17 *J. Lab. clin. Med.*, 1948, **33**, 1258.
18 Ibid., 1947, **32**, 320.
19 *J. Pediat.*, 1949, **35**, 58.
20 *Amer. J. med. Sci.*, 1946, **212**, 129.
21 *C. R. Soc. Biol., Paris*, 1939, **132**, 90.
22 *Amer. J. med. Sci.*, 1945, **209**, 306.
23 Ibid., 1944, **207**, 638.

mainly glandular. Allen and Kellner[13] have described the histological changes found in a pilot who was killed in an air crash one month after the onset of infectious mononucleosis: they noted areas of discrete focal mononuclear infiltration in many organs, including liver, kidney, heart, and brain. Custer and Smith[13] described the findings in nine fatal cases; that the tense engorged spleen is particularly liable to rupture in this disease is shown by the fact that this was the cause of death in four of their cases. These authors comment that "there are as many lesions of infectious mononucleosis as there are organs and tissues of the body." In five of their cases meningo-encephalitis was present, and peripheral neuritis in two others. Involvement of the central nervous system is not often diagnosed; Geliebter,[14] who described his findings in a child of 10 years, could only trace about a dozen examples in the literature. Tidy[15] has pointed out that benign lymphocytic meningitis and infectious mononucleosis with neurological manifestations may produce identical changes in the cerebrospinal fluid. Ricker and his co-workers[16] have described two fatal cases in which an acute ascending paralysis preceded death: in other organs there were histological changes to support the clinical diagnosis of glandular fever. Jaundice, too, has been recorded as an unusual complication, but Peterson[17] and De Marsh and Alt[18] have shown that liver-function tests may reveal abnormalities in a large proportion of cases despite the absence of clinically recognizable hepatic involvement. Peterson carefully compared cases with and without liver damage and could find no other distinguishing feature. Bower and his colleagues[19] in Los Angeles have obtained good results in the treatment of severe (anginose) cases of infectious mononucleosis with intramuscular injections of gamma globulin (4–8 ml.), and they suggest that this may be worth trying when jaundice is a complication.

Much has yet to be learnt about this disease, not least the discovery of its cause. Many authors have referred to its similarity to acute infectious hepatitis, and Havens and Marck[20] have shown that blood changes occur in experimentally induced hepatitis which closely resemble those of glandular fever. A virus is therefore the obvious choice as the aetiological agent. Van den Berghe and Liessens[21] have indeed recorded the infection of a monkey with blood from a patient, the blood changes which resulted being similar to those of infectious mononucleosis. Randolph and his colleagues,[22 23] however, have pointed out that blood changes similar to those of infectious mononucleosis may be found in cases of drug sensitization, though of course the Paul–Bunnell test is always negative. More detailed study of the epidemiology of the disease and of its clinical course will be required before there can be any certainty about whether infectious mononucleosis has a single cause or is a host reaction to a variety of causes.

ASSISTANTS IN GENERAL PRACTICE

If life could be started at the top it would be more enjoyable, but in medicine, especially, many years of training are needed before a man becomes his own master. In general practice some of the time is usually spent in assistantships, where close relationships founded on mutual trust must be established between men whose training has accentuated their self-reliance, decisiveness, and individuality. That misalliances are formed is not surprising, and from time to time many letters have appeared in this *Journal* testifying to the discomfort and resentment felt by assistants who have been unfortunate in their choice of principal. They have complained of overwork, too little time off for recreation, and of having to do too much night work. But the most substantial criticism has been of those principals who take on an assistant with a view to partnership and, while continually keeping open the possibility of partnership, always refuse to come to terms.

This problem among others is being studied by a special subcommittee of the General Medical Services Committee. Assistants are sitting on it, and have contributed much useful information about their difficulties. Incompatibility is inevitable sometimes, and the fault may well lie with the assistant rather than the principal —or with their wives. Clearly it is rash to enter into a partnership which may be life-long if the participants cannot get on together. But the assistants do not complain that partnerships are difficult to obtain: there is evidence that partners are now more often sought than assistants. Their charge is that the prospect of partnership is sometimes used merely as a bait. Abuse of this sort is undoubtedly rare, but it does exist. The B.M.A.'s Medical Practices Advisory Bureau has evidence of it, and does what it can to help assistants from being exploited. Doctors seeking assistantships would be well advised to do so through the Bureau, for it can give much helpful advice on suitable posts and on drawing up agreements.

A doctor would be unwise to become an assistant with view to partnership merely on the verbal understanding that he will eventually be offered a share in the practice. Yet an assistant told the subcommittee that in his experience most assistants have no written agreement. A legally drawn up document is advisable, but a written and agreed definition of the terms of the assistantship would seem to be the least precaution that principal and assistant should take. If the agreement includes a clause stating that at the end of a certain probationary period —for example, six months—both must decide whether they wish to enter into partnership—not necessarily immediately—then the assistant will have a reasonable safeguard. Though the irregular hours of work in general practice make it impossible to define explicitly

how much time off duty principal and assistant should have, any agreement should refer to it, for some assistants feel that they have been misled. An equal division of time off is a common practice, and if either party wants a different arrangement he should say so before the post is filled. Whether or not the assistant retains any fees for special services such as midwifery should also be made clear at the beginning, for practice varies. Some such arrangements as these, with advice from the Bureau when necessary, will be more effectual than books of rules and regulations in preventing assistants from being exploited. But the subcommittee will perform a useful task if it prepares a document giving general guidance to assistants and principals.

SARCOIDOSIS

Few diseases have attracted the interest of specialists in so many fields as has sarcoidosis. The range of clinical signs of the disease is now fairly well recognized, and it is known that the widely distributed lesions share a common pathology. Histologically sarcoidosis is characterized by focal proliferation of epithelioid cells, among which giant cells are commonly found. Central necrosis and caseation do not occur, and in the chronic stage hyalinization and fibrosis take place. The relationship between sarcoidosis and tuberculosis has caused much controversy. Some believe that the frequency of negative tuberculin tests in cases of sarcoidosis and the histological similarity between the two diseases indicate a direct relationship—the clinical and pathological differences being explained by variations of the immunity reactions of the body to infection with the tubercle bacillus. The other view, that sarcoidosis and tuberculosis are distinct diseases, is supported among other reasons because tubercle bacilli are not found in the lesions of sarcoidosis and the disease cannot be transmitted to animals. The recent discovery of a tuberculin-neutralizing factor in the serum of patients with sarcoidosis,[1] the suggestion that the inclusion bodies of sarcoidosis are related to an allergic hyperglobulinosis,[2] and the recognition of cases of erythema nodosum with radiological evidence of sarcoidosis within the thorax,[3 4] while of great interest, have by no means settled the question.

In the Bradshaw Lecture reproduced in the opening pages of this issue of the *Journal* Dr. J. G. Scadding puts the problems of this disease in clearer perspective. He rightly asserts that it is illogical to use selective criteria, such as a negative tuberculin reaction, in the diagnosis and subsequently to discuss the significance of such tests. It is clear that a clinical diagnosis of sarcoidosis must be made when a patient's symptoms and signs are characteristic of that disease. Pathological confirmation of the diagnosis depends on the demonstration in the various lesions of the histological changes referred to above. This definition wisely leaves open the question of aetiology. It is known that certain specific antigens, for example beryllium compounds, can produce the typical changes of sarcoidosis,[5 6] and it seems likely that the tubercle bacillus is another such agent. Probably other antigens, as yet unidentified, are capable of producing identical changes. New gains in knowledge have often resulted from the subdivision of a single syndrome into many diseases, and it may well prove that fuller understanding of sarcoidosis will be achieved in this manner.

Radiographs in pulmonary sarcoidosis show bilateral hilar lymph-node enlargement occurring alone or accompanied by diffuse pulmonary mottling in the lung fields. Snapper[7] was able to demonstrate that the lymph-node enlargement frequently preceded the pulmonary infiltration and often receded as the pulmonary infiltration progressed. This common sequence of events was confirmed in Dr. Scadding's series of cases, and it is evident that, although complete healing often takes place at a later date, the disease may progress to chronic pulmonary fibrosis with bulla formation. This serious development is often overlooked, and it is not known how often cases of pulmonary fibrosis may have originated in chronic sarcoidosis. Mallory[8] drew attention to a chronic granulomatous process of the lungs which gave rise to scarring and bullae, and he suggested that such changes resulted from sarcoidosis. The possibility that diffuse cystic disease of the lung associated with granulomatous changes might sometimes be caused by sarcoidosis has also been considered.[9]

The treatment of sarcoidosis has hitherto been unsatisfactory. Although many patients with pulmonary sarcoid suffer very little disability there is always the possibility that fibrosis, emphysema, and respiratory insufficiency may develop. Treatment is thus of great importance. Even if it is assumed that sarcoidosis is a manifestation of tuberculosis it would not be expected that streptomycin would be of value in a disease with lesions which are predominantly proliferative. Such scanty trial as has been made with this drug indicates that it is of no value in the disease.[10] Dr. Scadding has treated nine cases of pulmonary sarcoidosis with calciferol, using a dosage similar to that found effective in the treatment of lupus. Three of the patients were remarkably intolerant to the drug, but the six patients who were able to take full doses all

1 Wells, A. Q., and Wylie, J. A. H., *Lancet*, 1949, 1, 439.
2 Tellum, G., *Amer. J. Path.*, 1948, 24, 389, and 1949, 25, 85.
3 Kerley, P., *Brit. J. Radiol.*, 1942, 15, 155.
4 Skiold, N., *Acta. med. scand., Suppl.* 157, 1945.
5 Dutra, F. R., *Amer. J. Path.*, 1948, 24, 1137.
6 Agate, J. N., *Lancet*, 1948, 2, 530.
7 *Pseudo-tuberculosis in Man*, 1938, Haarlem.
8 *Radiology*, 1948, 51, 468.
9 Cunningham, G. J., and Parkinson, T., *Thorax*, 1950, 5, 43.
10 Pulaski, E. J., and White, T. T., *Arch. intern. Med.*, 1948, 82, 217.

improved. An exact interpretation of these findings cannot be given, and little can be deduced from so small a number of cases, but it seems that the use of calciferol in sarcoidosis is worth further clinical trial. Not only might it provide a useful and simple method of treatment, but it may also throw further light on the unsolved problems of this disease.

HEALTH ADMINISTRATION IN THE COLONIES

The evolution of medical and health administration in tropical colonial territories has been a steady process of transition from small beginnings to the complex organization found in the larger dependencies to-day. Little more than a century ago in a few countries, and appreciably less in the majority, Government medical services had their origin in military organizations or developed by the gradual assumption by Governments of some of the self-imposed tasks of medical missionaries and duties performed by doctors employed by commercial concerns. Little attention has been paid to this process of development, and comprehensive studies relating even to individual territories are rare; but one fact stands out above all others—the rate of progress has been astonishingly rapid. What has happened, in effect, is that centuries of progress by European standards have in the case of tropical countries been compressed into the life span of one or two generations, and it is not surprising if systems now in force vary and have not yet become fully stabilized. For the sake of efficiency health administration has had to follow whatever method of Government control is in force, and there is to-day an increasing tendency to decentralize to the provincial and district levels of government and to delegate executive authority over health matters to municipal and other local bodies vested with varying degrees of control over their domestic affairs. Similarly medical teaching is ceasing to be a departmental function as the Colonial universities successively achieve complete autonomy, and important medical research institutes are now virtually dissociated from departmental control.

At the top of the administrative tree the simple form of direct health administration by a director responsible only to the governor is being influenced by constitutional changes in government, and it is now not uncommon to find that direction of major policy is the responsibility of a lay member holding a position in the legislature analogous to ministerial rank in the United Kingdom. In fact the trend has been for the system of health administration to follow the pattern set in this country, but the progress has been so rapid by comparison, and conditions in the socially less advanced tropical countries differ so greatly from those in Europe, that weaknesses have inevitably appeared. While the ultimate success of any system of health administration must depend to a large extent on the calibre of the technical head of the department and his officers, the circumstances in which they carry out their duties are bound to have a strong influence for good or ill. Medicine in these days is becoming more and more a highly specialized science, and this tendency to specialization is adding another complication to the already difficult problem which faces the health administrator in the Tropics. He has not only to be capable of assessing the priorities of many urgent claims which are pressed on him for social, economic, or political reasons, but he must keep in close touch with developments in all fields of relevant research in order that the administration may not commit itself to a policy based on premises destined soon to be discarded. Further, he must possess a breadth of outlook not readily acquired or maintained by prolonged confinement in an office; he must travel widely, not only in his own domain but extra-territorially, to gain knowledge and sift the good from the bad in the experience of others.

One of the weaknesses of Colonial medical administration in the past has been that too many duties of a routine, non-technical nature have been forced upon medically qualified officers of all grades. They cannot be expected to maintain a professional competence and take the wide, objective view so necessary in planning for the future if they are harassed by routine duties which could readily be undertaken by lay members of the staff. This applies not only to administrative headquarters but also to all units in a service, and it is certain that decentralization will not succeed unless medical officers at the periphery are relieved of excessive non-technical routine duties whether in hospitals or in the preventive field.

In an article published elsewhere in this issue Dr. George Maclean draws attention to the possible unpreparedness of lay representatives on executive bodies for the responsibility of directing health policy that, whereas it is not actually thrust upon them, is being assumed by them. All those with experience of medical administration in the Tropics will agree with his insistence on the importance of health education. It is for those at present in executive charge of the health policy of the Governments, aided by expert advisers in this particular field, to see that this education is carried out and that it reaches every section of the population, especially the leaders. The Governments themselves should give serious thought to the advisability of proceeding with further decentralization and delegation of authority until they are assured that the ground has been fully prepared.

NEW MEDICAL BILL

In making it compulsory for medical students to work for a year in approved hospital posts before being licensed to practise independently the new Medical Bill, which is summarized at page 782, reflects the opinion of the medical profession to-day. The Goodenough Committee[1] recommended such an arrangement in 1944, emphasizing that "a person holding such an appointment should be regarded as a student who is consolidating his knowledge and widening his experience, and who still needs guidance and supervision." The B.M.A. agreed[2] that an "intern year" is desirable, and commented: "It should be a continuation of a basic general discipline in medicine that serves as a foundation either for training in a specialty or for general practice. It should not be regarded as a preparation for immediate independent practice. That preparation will come after registration, and its nature will depend upon the intentions of each individual." There may, of course, be some difficulty in putting this part of the Bill into effect if Parliament enacts it, and probably the posts will vary in quality at different hospitals. The intention that the internships should be educative must be kept to the fore, and they must never be allowed "to degenerate into a device for securing cheap resident service for hospitals or for staff."

The Bill prescribes machinery for appeal from decisions of the G.M.C., and this needs careful examination. When the Medical Disciplinary Committee—a new body to be set up—determines that a man's name shall be struck off the *Register*, he may appeal in accordance with the Bill's provisions within 28 days to the Judicial Committee of the Privy Council. At present there is no right of appeal. The B.M.A. has asked[3] for a right of appeal to the High Court of England. Correspondingly the appeal in Scotland would be to the Court of Session and in Northern Ireland to the High Court. The procedure in the Bill is more uniform, but it may have certain drawbacks. For instance, a further appeal to the House of Lords cannot be made from the Privy Council, whereas it can from the other courts. Again the expense of appealing to the Privy Council is likely to be greater than to the High Court. These objections may prove to be insubstantial, but they need considering. Welcome provisions in the Bill are that the Disciplinary Committee may take evidence on oath and that witnesses may be subpoena'd.

The Bill enables the Disciplinary Committee to make rules of the procedure to be followed and of evidence. It might well include a provision that complaints made to the Council should be supported by an affidavit or statutory declaration setting out the material facts. Some provision should also be included to make the Ministry of Health a party to a case by affidavit in order to prevent the present procedure by which the Ministry shelters behind some other plaintiff.

The provisions for direct representation of the profession on the G.M.C. are hardly adequate. There are now five Direct Representatives for England and Wales, one for Scotland, and one for Ireland. The Bill adds two more—one of them for England and Wales, and the other for Scotland. The B.M.A. has recommended that there should be a total of twelve—namely, seven for England, one for Wales, two for Scotland, one for Northern Ireland, and one for the Irish Republic. Medical men are not alone in desiring direct representation on disciplinary and administrative bodies, and the principle is one that should command respect in the House of Commons. The Association also recommended that a Penal Cases Committee should be set up as well as a Disciplinary Committee. The Penal Cases Committee would examine the evidence and decide whether a case should be heard. Members of this committee would not be allowed to sit in the Disciplinary Committee on those cases that they had already examined. This would seem to be a safeguard worth including in the Bill. Nor is it clear how frivolous charges are to be prevented from coming before the Disciplinary Committee. The Disciplinary Committee provided for in the Bill consists of the President and eighteen other members of the G.M.C. It is questionable whether this body is not too large. If the committee consisted of twelve members it would be much less unwieldy, discussion likely to be less confused, and the defendant not so embarrassed.

[1] *Report of the Interdepartmental Committee on Medical Schools.* H.M.S.O., 1944.
[2] *The Training of a Doctor.* 1948.
[3] *British Medical Journal*, 1947, 1, 81.

MACROCYTIC ANAEMIA IN LIVER DISEASE

In 1936 Wintrobe[1] concluded from his observations on 132 patients that macrocytic anaemia in cases of hepatic disease resulted from an inability to store the necessary haemopoietic principle, and most other workers at that time held the same view. In recent years the greatly increased incidence of acute hepatitis together with experimental work on liver disease has led to some re-examination of this clinical problem. The occurrence of a macrocytic anaemia in both acute hepatitis and cirrhosis has been confirmed, but the older explanation for this is now doubted. Meulengracht and Gormsen[2] have analysed their findings in 150 patients suffering from that form of subacute and chronic hepatitis which has been so prevalent in Denmark since about 1943. The majority had some degree of anaemia, but unfortunately determinations of the so-called absolute values were not made and estimates of cell size have to be based on the colour index, which is likely in this condition to be even more unsatisfactory than usual in the detection of changes in the red cells. The average colour index was reported to be 1.1 (which was regarded by the authors as normal), but there can be no certainty that the cells were not increased in volume, since simple swelling which would be shown by a rise in mean corpuscular volume and a fall in mean corpuscular haemoglobin concentration would leave the colour index unaffected. Direct measurements of the diameters of cells suspended in their own serum showed, in fact, that in more than 50% of these cases the mean diameter of the cells exceeded 8μ (the accepted upper limit of normal for this method). There appeared to be no correlation between

[1] *Arch. intern. Med.*, 1936, **57**, 289.
[2] *Blood*, 1948, **3**, 1416.
[3] *Acta med. scand.*, 1949, **133**, 321.
[4] *J. clin. Invest.*, 1949, **28**, 286.
[5] *Blood*, 1949, **4**, 511.
[6] *The Distribution of Red Blood Cell Diameters in Liver Diseases*, 1948, Oslo See annotation in the *British Medical Journal*, 1949, **2**, 1401.

the mean cell diameter and the icteric index, degree of anaemia, or colour index. Marrow examination disclosed slight hyperplasia of red-cell precursors but no evidence of a megaloblastic type of erythropoiesis. In no case in which it was tried was there any response to injections of liver extract. Meulengracht and Gormsen believe that the macrocytosis may be at least partly due to changes in the plasma—for example, an increase in the concentration of bile salts, with consequent swelling of the red cells. Lindgren[3] has reported a close relationship between the variations in mean cell diameters and serum bilirubin values in a number of cases of acute hepatitis.

Jarrold and Vilter[4] carried out a full investigation of 30 patients with portal cirrhosis and found a macrocytic anaemia in 65% (and in the majority a reticulocytosis of up to 8%), with mean corpuscular volumes mostly in the range 100–110 cu.μ. Apart from three patients who were suffering from gross nutritional deficiency none showed any significant improvement following administration of liver extract or folic acid. The three who responded were also the only patients who were found to have megaloblasts in the bone marrow. These workers conclude that the macrocytic anaemia of chronic liver disease is caused by a metabolic defect entirely different from that responsible for pernicious and allied macrocytic anaemias, but do not offer any suggestions about its nature. A similar study of blood and bone marrow in 25 cases of portal cirrhosis by Berman and his colleagues[5] showed that the majority had a macrocytic anaemia, the severity of which was not related to that of the disease. Hyperplasia of the marrow was a feature, but in none of the cases was there a megaloblastic type of red-cell production. The view is favoured that haemolysis may be a cause of the anaemia, and some abnormality of the spleen is suggested as a possible factor. We have already referred in an annotation to Larsen's very detailed investigation,[6] which led him to the conclusion that in all cases with damage to the liver parenchyma the red-cell diameter is increased while the mean corpuscular volume remains normal. He believes this to be due to the production of larger cells by the bone marrow, though the mechanism of their formation is not the same as in pernicious anaemia. Further work is necessary before the correct explanation can be given for the facts which have recently come to light. Lines of investigation worth following would seem to include the relationship of the anaemia to changes in total blood volume and of the macrocytosis to such factors as the concentration of bile salts and *p*H, together with further detailed serial studies of individual cases with the object of showing whether macrocytosis arises only in newly formed cells or whether it affects those already in circulation.

PROCAINE PENICILLIN PREPARATIONS

It cannot yet be said that the best methods of administering penicillin are generally agreed on, particularly for patients in whom more than one, or at most two, daily injections are impracticable. Such patients include almost all in their own homes and a large number of hospital out-patients, and the problem of how to treat these patients adequately has in the past been difficult. The advent of the procaine compound of penicillin, which owing to its much lower solubility is far more slowly absorbed, has to a great extent overcome this. Not long after the introduction of the original procaine penicillin preparation—a simple suspension in oil which, it was claimed, kept the penicillin in the blood at an effective level for 24 hours—it was proposed to retard absorption still further by adding aluminium stearate, which has a water-repellent effect: from a depot of this material absorption was said to continue for three days. Griffiths and his colleagues[1] at St. Bartholomew's Hospital tried the effect of administering such a preparation at 2-day intervals and were dissatisfied with the clinical results: it seems that the policy of prolongation of effect from a single dose may perhaps be carried too far, the levels attained during this long period being presumably sub-optimal. On the other hand, Peacock and Gillespie,[2] by giving a large dose of such a preparation (2,000,000 units in 6.6 ml.), obtained satisfactory levels for 6–7 days in bed patients and for 4–5 days in ambulant subjects.

Mr. E. Griffiths, Mr. A. J. Walker, and Dr. R. A. Shooter report in this issue (p. 761) a further study on the same lines, having used for the purpose the abundant clinical material available in a large hospital out-patient department. Such material is not often systematically studied, but it is worthy of attention in that it represents a large proportion of the conditions in which penicillin is most useful, both in restoring function rapidly and in preventing the more serious consequences which used to follow such lesions. It is possible by accurate assessment of the extent of the lesion and by careful recording of the time required for relief of pain and for eventual healing to use these infections for determining the value of different forms of treatment; such direct assessment is more significant than more theoretically based methods, such as, for instance, the simple study of the blood levels attained. The conclusion from the present series is that a new preparation embodying 1% of aluminium stearate but also including sodium penicillin gives results as good as those previously obtained with the ordinary preparation of procaine penicillin in oil or with the same dose of sodium penicillin in saline given twice daily.

Finality has probably not yet been reached with preparations of this kind. Oil suspensions in general, and particularly those containing larger crystals of procaine penicillin, require the use of larger needles; even so they have sometimes given trouble from blockage. It is possible to dispense with oil altogether and administer procaine penicillin in suitable form as a suspension in water, though here again particle size is an important factor. The addition of sodium penicillin to give an immediate and more vigorous effect is probably a wise policy and likely to be continued. Doubtless such preparations will be improved both in convenience of administration and in certainty of effect, and a single daily dose of a volume of 1 ml. should serve well for the treatment of all ordinary and fully sensitive infections. Only in this way can the patient who cannot be seen more than once daily be afforded continuous protection.

[1] *British Medical Journal*, 1949, 2, 958.
[2] *Lancet*, 1950, 1, 495.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

HEADACHE

BY

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Headache is perhaps the commonest complaint in medicine and it often presents a delicate problem of clinical diagnosis, calling upon all the doctor's knowledge and experience. The difficulty is that the significance of the symptom is so varied. As Wolff has written in the introduction to his recent book, "Though there are few instances in human experience when so much pain may mean so little in terms of tissue injury, failure to separate the ominous from the trivial may cost life or create paralysing fear."

Even if we knew the essential cause of headache it is doubtful whether it would be of much practical help, because the primary causes are so diverse. To attempt here to refer to any large number of them individually would be bewildering, and it seems better to treat the subject in rather general terms, making special reference to recent work.

Aetiologically, headache may depend on: (*a*) abnormal conditions within the cranium or on the scalp (including migraine and high blood pressure); (*b*) abnormal conditions in other parts of the body producing headache by toxic or other means; and (*c*) psychological factors. The doctor's first problem is obviously to determine whether he is dealing with any physical disease or abnormality, or whether the headache has a psychological basis. Diagnosis by a process of exclusion is both dangerous and unsatisfactory, and most headaches, even the psychological, have their positive diagnostic features. Nevertheless, it is necessary in all cases to exclude the most important of the organic causes.

As soon as we begin to think of individual cases it is at once evident that the doctor's assessment will be greatly influenced by the age of the patient. Whatever this is, the doctor asks himself, consciously or unconsciously, to which class the headache is likely to belong, but the probable causes under each heading differ according to the age of the patient. For example, tuberculous meningitis and poliomyelitis in the first group, or measles in the second, may have to be seriously considered in the child, but are not given a thought in the case of an elderly patient. Such a process of sorting goes on in the trained mind more or less unconsciously. It is continued, still more or less unconsciously, by observations under two headings: (1) the features of the symptom itself; and (2) associated phenomena. In other words, he takes a careful history and makes a thorough general examination of the patient.

Mechanism of Headache

The essential mechanism of the symptom is unknown, but the researches of Wolff and others in America and of Pickering in this country have added much to our knowledge of those headaches that have a basis in organic disturbance, and even of some that are primarily psychological. This recent work has emphasized the role of the blood vessels within the cranium as pain-sensitive elements, but the scalp, the trigeminal nerve, and the meninges play important parts in the mechanism of many headaches. It is, of course, through cerebral function that the pain comes into consciousness, but all are agreed that the brain tissue as such is not sensitive, and it is believed that the pain that may result—for example, from vascular lesions within the brain—is excited by pain receptors on the blood vessels.

It has been shown that stimulation of a pain-sensitive structure in the part of the cranium above the tentorium leads to headache mediated by the trigeminal nerve and referred to the anterior part of the head—that is, in front of a line joining the ears across the vertex—while pain provoked in a similar manner from structures below the tentorium is chiefly felt posteriorly, being mediated by the upper three cervical nerves and to some degree by the glosso-pharyngeal nerve. Most headaches arise from disturbances of vascular structures, the main mechanisms at work being distension, dilatation, and traction applied to intracranial arteries. Rarer causes are displacement of venous sinuses, local inflammation affecting pain-sensitive structures, and irritation of the nerves concerned.

The headache experimentally produced by the intravenous injection of 0.1 mg. of histamine phosphate has been extensively studied and has been shown to depend on dilatation, stretching, and increased amplitude of pulsation in the larger basal arteries and their branches, and pyrexial and many toxic headaches have a similar mechanism. It is suggested that even the headache of brain tumour probably originates chiefly in distortion of cerebral blood vessels; it is not directly related to the intracranial pressure, though rapid changes in the pressure often provoke headache of considerable severity.

Headache Due to Local Disease

The headache of organic brain disease is above all a morning headache; it is present daily or almost daily when the patient wakens in the morning and passes off in the course of a couple of hours or so. It is quite true that at a later stage it is, as used to be taught, present also if the patient wakens in the night, but now most cerebral tumours are diagnosed before that stage is reached. This is not an intracranial-pressure headache, for it occurs with many cerebral lesions when the intracranial pressure is normal. The pain may be frontal or occipital, according to the site of the lesion and the presence or absence of severe intracranial pressure. Occasionally it is more localized and then it may also be more continuous, being probably more directly related to the site of the lesion. In the early stages the headache is seldom accompanied by vomiting, but at a later stage vomiting or retching occurs occasionally in the morning with the headache and may be accompanied by nausea. The vomiting occurs at an earlier stage with cerebellar tumours than with other progressive intracranial lesions.

As regards associated features, any abnormal sign in the nervous system, even inequality of the pupils, may be of great diagnostic importance, but even in the absence of all abnormal signs, a history of the occurrence of a fit, focal or general, or of any disturbance of consciousness or speech, or any mental failure or lapse, or of any complaint of awkwardness in a limb, or any disturbance of sight is of the highest importance, and suggests strongly that the headache may have its basis in organic cerebral disease. The headache that occurs after cerebral injury

has less well defined characteristics, but, however else it may be brought on, it is usually precipitated by stooping and physical effort, and by efforts at mental concentration.

Headache associated with high blood pressure sometimes presents all the features of the headache of intracranial disease. In occasional cases the acute aggravations associated with hypertensive encephalopathy may lead on to convulsions and coma, from which the patient makes a good recovery as the crisis subsides.

The headache of meningitis or meningeal irritation, accompanied, as it soon is, by stiffness of the neck, rise of temperature, and fever, seldom presents any difficulty in diagnosis in the adult. In the child stiffness of the neck and Kernig's sign should always be tested for when prostration and fever are present or in the presence of an epidemic of poliomyelitis.

Diseases of the skull are nowadays uncommon, with the exception of mastoid disease, but one should never fail to test for mastoid tenderness in the young subject. Sinusitis, not only of the frontal sinus but also of the maxillary antrum or of the more deeply placed sphenoidal and ethnoidal sinuses, is another important cause which has to be mentioned here. This subject has been dealt with by Mr. C. Gill-Carey in another article of this series (February 18, p. 427). Some tenderness over the maxillary or frontal sinuses will probably be present.

Rheumatic conditions of the scalp, and of the muscles at the back of the neck, are quite an important cause of headache, and, as the pain is usually present when the patient wakens in the morning, these headaches may closely simulate those of intracranial disease. Usually, but not always, arthritis is present in the cervical spine and the headache is mostly occipital. However, with fibrositis of the scalp the pain may be further forward and the headache may be very intense: it is usually accompanied by some local tenderness or by sensitiveness of the scalp and hair. Injury of the scalp is a factor in some cases of post-traumatic headache.

Wolff and others have emphasized the importance of superficial structures in regard to the headache of migraine. It seems to be established that the pain of migraine can be abolished by injection or section of the trigeminal nerve: in many instances only the supraorbital branch and/or the auriculo-temporal branch need be interrupted. Pressure on the external carotid artery or on the temporal artery may relieve the pain, as may also in some cases interruption of the sympathetic nerve supply to the arteries of the affected side of the head. Such measures do not prevent the occurrence of the visual disturbance or other sensory phenomena which may precede or accompany the onset of the headache, and these almost certainly have their basis in disturbances of arteries on the cerebrum itself.

The diagnosis of migraine presents no difficulties when the whole syndrome is present, but when the headache is not predominantly unilateral and is not associated with vomiting the diagnosis from other varieties of "functional" headache may be very difficult. The degree of prostration and the response to an injection of ergotamine tartrate may help with the diagnosis. The diagnosis may also be difficult when an attack of migraine lasts for a very long time or the patient develops a condition of almost continuous headache—what might be called status migrainosus. It is obvious that in such cases the strictest care must be taken to exclude the possibility of organic disease within the cranium. If the pain in migrainous attacks over years is always on the same side, the possible presence of an organic vascular abnormality has to be borne in mind, and the occurrence of any abnormal sign such as slight proptosis, or any ptosis or ocular palsy associated with the attacks, would greatly increase the possibility of such an abnormality. Numbness referred to one side of the face, or tongue, and to the fingers may occur in the early stage of a migraine attack, but if numbness more extensive than this is present it is possibly due to an organic vascular abnormality, which may call for treatment.

Headache Due to General Disease

Headaches that are due to disease or abnormality in other parts of the body or to general infections or intoxications are very numerous, and it is impossible here to consider any large number of them; the majority present little difficulty in diagnosis because of the prominence of other associated symptoms. Kidney disease occupies first place, and as it usually comes on insidiously it may be overlooked, unless the urine is tested as a routine measure in all cases of recurring headaches. Typhoid fever and syphilis are other conditions—both less common now than formerly—in which the associated symptoms may be slow in making their appearance. In some patients who are headache-prone constipation may be either the cause or an important precipitating factor. Anaemia is a cause to be borne in mind, and, equally, the iron that may be given for its treatment. Another common drug that may produce headaches is strychnine. The histamine headache, somewhat mysterious in its causation, is usually unilateral and clinically resembles migraine (see below).

Psychological Headache

Wolff, though he has spent much time and effort on the investigation of headaches of "organic" origin, recognizes that "the vast majority of discomforts and pains of the head stem from readily reversible bodily changes or are accompaniments of resentments and dissatisfactions." He might have added anxieties and depression. The psychologically determined headache is often difficult to diagnose with confidence, but in most cases it has well-defined characters. It is most important that no leading questions should be asked about its quality, but if the patient is simply allowed to talk of his symptoms or asked to describe his headache he will refer to a feeling of tightness round the skull, or to a pressure on top of the head, and to a feeling of tiredness in the eyes. These varieties are constantly associated with anxiety. The hysteric may complain of an intense boring pain at the vertex. More difficult to be sure of are the pains at the back of the head, or in the forehead, associated with depression.

Many headaches that are really of a functional nervous origin are put down to other causes which are at most subsidiary, such as eye-strain, mental concentration, lack of fresh air, and so on, and many pairs of needless and useless glasses are prescribed for patients suffering from the feeling of tiredness in the eyes characteristic of the anxiety state. All the slighter functional nervous headaches come on during or after the day's work, but the more severe are more continuous.

The headache that never goes away and the headache on which aspirin has absolutely no effect are likely to be psychogenic; all "organic" headaches, even that of meningitis, are relieved to some extent by aspirin and similar drugs. Psychological factors play a part in many other headaches—perhaps in all. It seems to be established that in many patients attacks of migraine are precipitated by psychological influences. Wolff is of the

opinion that in many cases of emotional disturbance—for example, anxiety—the state of tension in the muscles at the back of the neck is responsible for causing headache.

A very interesting observation on the other side of the account is that in some cases of severe head injury with damage to the frontal lobes the patients are euphoric and do not seem to suffer from headaches. This makes one think that the associated depression is often a factor—perhaps a considerable factor—in post-traumatic headaches. In fact it is a matter of the greatest difficulty to determine when post-traumatic headaches cease to be due to organic causes and are carried on by psychological influences, and there is certainly a wide margin of overlap between the organically determined and the psychologically determined post-traumatic headaches.

Treatment

While it may be trite to say that the treatment of the symptom is to remove the underlying cause, it is nevertheless a fundamental truth and nothing can condone a neglect to try to discover the primary disturbance responsible for headaches. However, whether the cause can be discovered or not, and whether it is removable or not, there are many instances in which treatment has to be symptomatic.

In the worst cases—for example, meningitis—drugs of the morphine group should not be withheld, but equally they should not be given in cases of recurrent headaches or when the illness may be of indefinite duration. There are now three types of synthetic analgesics available—namely, the aspirin, pethidine, and "physeptone" groups. The former is still the most generally useful, and the various preparations in which it is combined with phenacetin and caffeine or with codeine are well known. Occasionally it is combined with a small amount of cascara to counteract its constipating effect, and there is something to be said for this, but generally a separate laxative will be required in any case. The other two groups of pain relievers are excellent for treatment of short duration, but unfortunately they both are habit-forming, and pethidine in particular gives rise to a very unpleasant addiction and should be used guardedly with this fact in mind (100 mg. three-hourly). Phenobarbitone, which is often given, has little or no value as a pain reliever but acts as a general sedative and hypnotic.

Of the headaches due to intracranial causes the most troublesome in practice are, (1) those following head injuries, and (2) migraine. For the former no satisfactory treatment has yet been found. The immediate cause of the headache is unknown, but it is generally conceded that it has a basis in organic disturbance: in many cases depression and anxiety complicate the picture before long and are aggravating influences of the headaches; and efforts at mental concentration may also induce headaches. So long as other elements of the post-concussive syndrome—particularly the mental inactivity and difficulty in concentration—continue, it is best to regard the headaches as "organic" in origin, unless other influences are obvious.

In general, rest in the horizontal position is the best treatment when a headache comes on; analgesics of the aspirin group usually give relief, but in some cases they seem to aggravate, possibly by causing increased pulsation in cerebral or cranial vessels—5 gr. (0.32 g.) may relieve and 10 gr. (0.65 g.) aggravate. Phenobarbitone, ½ gr. (32 mg.), given two or three times in the day over a long period as a general sedative may help to reduce the liability to headaches. The certainty of cure can always be held out to the patient, and he needs encouragement in his home. In some cases too much sympathy may be a mistake, but it is a mistake not often made, for the conditions are trying for all. It should not be forgotten that even when the headaches are greatly influenced by psychological factors they are nevertheless post-traumatic.

Migraine obviously calls for two kinds of treatment—the immediate treatment of the attack and the long-term treatment of the liability. For the headache once established there are no new effective remedies, and ergotamine tartrate by injection remains the one remedy that is efficacious in a fair proportion of cases. If it can be given before the headache is established its efficacy is higher, and, provided vomiting does not set in early, simpler remedies such as a Seidlitz powder followed by aspirin, 10–15 gr. (0.65–1 g.), are often very helpful. Tablets of ergotamine tartrate may be of service in this stage, but are perhaps more valuable if taken every night for a time as a prophylactic.

The long-term treatment is that of the vasomotor instability which is responsible for the attacks. Some physicians think this in turn is due to allergy, and tests may be done to find the offending substance. There are various proprietary drugs on the market for which merit is claimed as vasomotor sedatives, but I have not found anything better for this purpose than the combination of phenobarbitone and thyroid: ¼ gr. of each may be given in the morning, and ¼ gr. of thyroid and 1 gr. of phenobarbitone at night, over a period of three to four months. The adjuvants of fresh air and exercise are not to be neglected, and, as the sufferers have usually obsessional personalities, frequent short holidays are helpful. In a few cases, as already indicated, surgical procedures have been tried, but the results still await final evaluation.

Among the second group of headaches (toxic and other) the histamine headache, to which reference has already been made, is of relatively recent recognition. It is similar to migraine and an attack can be precipitated by subcutaneous injections of 0.1–0.2 mg. of histamine acid phosphate. Very good results have been obtained by desensitization by graded subcutaneous injections of this preparation, increasing in the course of a few days from 0.05 to 0.1 mg., and continued twice daily for three to four weeks. Antihistamine drugs are on trial and new ones are being introduced almost monthly, and they are certainly effective in a proportion of cases.

The psychological or neurotic headaches are among the most difficult to treat, involving as they usually do not only factors of personal nervous and mental constitution but also social problems. In some cases due to anxiety, social adjustments can be made and the patient can be relieved of responsibility, with great relief of his or her headaches. In cases of periodic depression the headaches are likely to pass with the depressed phase, and meanwhile drugs of the amphetamine group may help. In all cases physical factors must be sought for, and the urine must be tested. In some cases headache which is primarily psychological may have a physical mechanism. Wolff and others believe that tension in the muscles of the neck, long sustained as the result of emotion, is the means by which headache is produced in many psychological cases, and, if so, massage and the practice of relaxation may give relief. Specialized psychiatric treatment is called for in some cases, and if the patient can accept the proposition that his headaches have a psychological basis he may be able to improve his social adjustments, or the recognition may enable him better to endure his afflictions.

THE SCIENTIFIC METHOD

SIR HENRY COHEN'S HARVEIAN LECTURE

The Harveian Lecture was delivered before the Harveian Society of London on March 22 by Sir HENRY COHEN, Professor of Medicine, University of Liverpool, whose theme was "Harvey and the Scientific Method." No compliment, he said, could be more acceptable to a physician than an invitation to deliver a lecture associated with the name of Harvey, one of the greatest physicians of all time, not because he discovered the circulation of the blood, but because he demonstrated beyond all reasonable doubt that the blood circulated. But with already a hundred such lectures delivered before the Society, and very many more before the Royal College of Physicians, the task became increasingly difficult. Some lecturers had solved the difficulty by avoiding it and omitting Harvey from their discourse, and others had observed, with a French writer, that everything had been said before but nobody had listened, and so it might be said again.

Methods of Belief

There were four methods (the lecturer continued) on which belief or doctrine might be based—namely, the methods of tenacity, of authority, of intuition, and of science or reflective inquiry. Tenacity, obstinacy, perseveration—call it what one pleased—was the basis of many medical doctrines commonly held to be true. A glance at medical textbooks made it plain that habit or inertia made it "easier to continue to believe a proposition simply because we have always believed it." Fables about the value of certain drugs or diagnostic measures persisted because the mind was closed to all contradictory evidence. History might not repeat itself, but writers of textbooks did, and their reiteration, whether true or false, strengthened the prevailing belief.

The second method, that of authority, consisted in an appeal to an accepted source which in the highest degree might be regarded as infallible. Two forms of appeal to authority must be clearly distinguished. One was reasonable and inevitable in the practice of medicine. No man had time, even if ability, to find out all knowledge for himself; he accepted, for example, the pronouncement of experts on the carbohydrate values of foodstuffs, or the significance of electrocardiographic patterns, or the fact that herpes zoster was a virus infection. But he should retain the right to question authorities if his experience led him to doubt their statements; there were other authorities to whom he could appeal, and indeed he could acquire competence and experience himself with which to test the validity of authority.

Appeal to Authority

The second form of appeal to authority brought in an external source which was invested with the right to give sanction to beliefs. This was the basis of much of our religion and politics, and in the history of science it had played a sinister and obstructive role. It was most strikingly exemplified in the sentence of the Inquisition on Galileo in 1633—five years, by the way, after the publication of Harvey's *De Motu Cordis*. At that time the methods of tenacity and authority dominated anatomy and medicine. The purpose of discussion in Harvey's time was not to discover new facts but, in medicine, to demonstrate the truth of Galenic teaching. Any chapter in the history of human thought would reveal that there could be no uniformity or stability of belief for *Homo sapiens*—a species which did not include all men, or for the inquiring and inquisitive mind, which was based on authority. As for the third method, that of intuition, intuitions were self-evident only within an accepted framework. It was at one time "self-evident" that the earth was flat and that the sun moved round the earth. For most propositions self-evidence had been quoted, yet it was not difficult to establish that current knowledge played a large part in intuition, and the certainty and authority with which intuitions were uttered were no guarantee of their validity.

It was the fourth method—the scientific method—which was pertinent to his theme. There were certain aspects of the scientific method which in relation to Harvey's work needed some elaboration. It was customary to describe three main stages in arriving at a scientific truth: (1) the observation of significant facts, (2) the formulation of a hypothesis which if true would account for those facts, and (3) the deduction from the hypothesis of consequences which could be tested by observation or experiment. The first stage of most discoveries, from Archimedes with his screw to Alexander Fleming with his mould, was a chance observation. But a chance observation lit the spark only in the mind of genius, which responded to it by a tentative hypothesis. There must be critical discrimination in the selection of apposite data. Face values must not mislead. It was the mark of scientific ability to be able to distinguish the significant facts. In other words, the observation of significant facts was not uncontrolled observation, but observation with a purpose. When the significant facts were assembled possible explanations were formulated, an attempt was made to produce order out of chaos. Every science was interested in systems and generalities. It was here that formal logic played its part; but formal logic was not a scientific method, it was an instrument which demonstrated that if certain propositions were true others were also true, but it did not establish the truth of the initial premise.

To recapitulate, the stages in the method of science as exemplified by its history were (1) the chance observation; (2) the tentative hypothesis; (3) the search for significant facts which confirmed or refuted the tentative hypothesis or led to further hypotheses—the process of induction—which then could be tested by observation and experiment, or the process of deduction.

Galenic Beliefs Disputed

With this scheme of belief in mind, Sir Henry Cohen turned to the contribution which Harvey had made to the knowledge of the heart and blood vessels. Until his day, and indeed for many years afterwards, in the places where the methods of tenacity and authority held sway, the universal doctrine was that of Galen. Here the lecturer illustrated diagrammatically the Galenic conception of the circulation. The Galenic view had been disputed before Harvey, notably by Servetus, in a work published in 1533 but written earlier; also by Prosper Albinus, a professor of Pisa, who came closest to Harvey's views and published two interesting books, in 1571 and 1593, in which he described the valves of the heart, saying that the heart in systole propelled blood in the aorta and pulmonary artery, and in diastole received blood from the vena cava and pulmonary vein.

But whatever contributions these and others might have made to the idea of the circulation of the blood, they were insignificant when compared with Harvey's. He stood alone by virtue of his methods rather than of his discovery, great as the latter was in its repercussions on medicine. The seeds were sown by the University of Padua, which played an immense part in freeing Harvey's mind. Of all European universities it was least shackled by empiricism. There the experimental and quantitative methods of investigation were early introduced into the physical and biological sciences. The question "How?" in Padua assumed greater importance than the question "Why?" A university which had sheltered Copernicus and Galileo had naturally a strong mechanical bias. Thus it was that Harvey proposed both to learn and to teach anatomy, not from books, but from dissections, not from physicians and philosophers, but from the fabric of nature. That Harvey should turn to the heart for his major interest could cause no surprise. With Aristotle, he regarded the heart of animals as the foundation of life, "that upon which all growth depends and from which all power proceeds."

Harvey had been tutored in the Galenic doctrine of the veins filled with "natural spirit" and the arteries with "vital spirit," but, having made the inference that if the blood of the arteries and of the veins was the same there must be somewhere continuity between the arteries and the veins, he sought the significant facts. First he disposed of certain hypotheses by revealing their inconsistencies with known facts. Indeed, the introduction to *De Motu Cordis* was a critical review of former work. In the true spirit of science he isolated from a mass of irrelevant observations and considerations the one which was

amenable to scientific treatment—namely, the mechanics of the heart. His predecessors had asked "Why?"; Harvey asked "How?" and only occasionally did he deviate from that central question. Merely to ask the question, let alone to answer it, was a remarkable innovation.

Harvey turned to comparative anatomy and embryology, and argued from fishes and amphibians and again from the human foetus, leading up to the conclusion that the passage from the vena cava to the aorta was accomplished through the substance of the lung. After showing how Harvey upset the conceptions of the circulation which persisted until his time, the lecturer added, "So clear are his observations and so cogent his reasoning that I would insist that every medical student had *De Motu Cordis* as a set book for his preclinical study."

Harvey's Achievement

It was true that there was a missing link in Harvey's demonstration. The channels of communication between the arteries and veins had not been demonstrated; they remained to be revealed by Malpighi in 1661. In retrospect it seemed strange that Harvey did not himself prove by simple but crucial perfusion experiments the continuity of the passage. But his wonderful book of the seventeenth century—a book which, as Michael Foster said, was one consistent and continuous argument, an argument founded not on general principles and analogies but on the results of repeated appeals to vivisection and ocular demonstration—did more than achieve its scientific purpose. It attacked and laid bare the shallowness of the conventional mind. It pressed the acceptance of rational truth. If he were to describe the mind of Harvey he could do no better than adopt the words of one of Harvey's patients, Francis Bacon, who wrote, not of his physician, but of himself—a flattering self-portrait—as having a mind flexible enough to catch the resemblances of things and at the same time to study and fix and distinguish their subtle differences.

"In the turmoil in which we live," said Sir Henry Cohen in conclusion, "we who practise and teach medicine and try to fashion its future have a great need for the refreshing cultural diversion to be found in literature and scholarship, yet in our calling the time which we devote to reading, research, and meditation becomes less as the complexity of our lives increases. I have taken advantage of the opportunity which this occasion presents to put forward judgments upon a philosophic theme, but I pray my critics will in justice remember, what I shall certainly not forget, that these are, in the nature of things, the work not of an expert but of an amateur."

NEW MEDICAL BILL

EDUCATION AND THE G.M.C.

The Medical Bill, the text of which was published on March 23, was introduced in the House of Lords on March 22 and given a formal first reading.

The Bill makes provisions designed to improve the standard of medical education in accordance with the 1944 recommendations of the Goodenough Committee. There are some changes proposed in registration, in the composition of the General Medical Council, and in the procedures governing professional discipline.

The full title is "An Act to amend the Medical Acts, and for purposes connected therewith." Clause 1 provides that, before becoming fully registered and entitled to set up in practice, a medical student who has passed his final examinations must spend at least a year as a resident in one or more approved hospitals or institutions. The period, "not being less than 12 months," will be prescribed by the regulations of the General Medical Council approved by order of the Privy Council. A certificate will be required stating that the student has been engaged for such minimum periods as may be prescribed in medicine and in surgery and "that his service while so employed has been satisfactory." Any time spent engaged in midwifery during this period may be counted either under medicine or under surgery, as the student may elect, but the G.M.C. will indicate in its regulations the maximum period which may be counted for this purpose. Once a student has passed his final examinations he will be provisionally registered on payment of the appropriate fee.

The provisional *Register* will be kept separate from the main *Register*, and once full registration is achieved the person's name will be removed from the provisional *Register*. Provision is made for the separate publication from time to time, as the G.M.C. may direct, of the provisional *Register*. These provisions are to apply also to anyone holding a qualifying diploma granted by a university or other corporation in the Republic of Ireland, and for this purpose the approved hospitals will include those approved by the Medical Registration Council or some body acting on behalf of that Council in Ireland.

General Medical Council

The Bill also provides for an increase in the membership of the G.M.C. from 39 to 45. His Majesty the King will nominate five members who are registered medical practitioners and in addition three laymen—two for England and Wales and one for Scotland.

The Royal College of Obstetricians and Gynaecologists will now be included among the colleges and other bodies specified in Subsection (1) of Section 7 of the Medical Act of 1886. Those members of the Council elected by medical practitioners resident in England and Wales will be increased to six and those elected by medical practitioners resident in Scotland will be increased to two. It is also provided that no person shall be disqualified from membership of the House of Commons by reason of being a member of the General Medical Council. M.P.s who are on the Council, however, are not to be remunerated for sitting on the Council.

Hitherto the correct title of the Council has been "the General Council of Medical Education and Registration of the United Kingdom." Henceforward the usage which has been common for so many years will have statutory approval and "the Council shall be called the General Medical Council."

Discipline

The main disciplinary provision is one which has been much discussed over the past few years. The Bill provides for the setting up of a Medical Disciplinary Committee, to which will be transferred all the functions of the Council under Sections 26 and 29 of the 1858 Act. This committee will be composed of the president and 18 other members of the General Medical Council, of whom at least six shall be elected members of the Council and at least one a layman. The committee will be appointed by the Council, and a quorum will be nine. Where there is a complete division of opinion the chairman, in addition to his vote as a member of the committee, shall have a casting vote. Normally the chairman of this committee will be the president. For the purpose of its proceedings the committee may administer oaths, and "any party to the proceedings may sue out writs of sub poena ad testificandum and duces tecum."

For the purposes of advising the committee on questions of law there will be an assessor to the committee, a barrister, advocate, or solicitor of not less than ten years' standing appointed by the Council. The Lord Chancellor may make rules as to the functions of these assessors.

Clause 16 reads as follows:

"16.—(1) Section twenty-nine of the Medical Act, 1858 (which provides, among other things, for the erasure of the name of a medical practitioner from the register on conviction), shall have effect as if for the words from 'in England' to 'crime or offence' there were substituted the words 'by any court in the United Kingdom or the Republic of Ireland of any felony, misdemeanour, crime or offence.'

"(2) For the purposes of any inquiry under the said section twenty-nine whether a person has been guilty of infamous conduct in any professional respect, a finding against him in any matrimonial proceedings in the United Kingdom or the Republic of Ireland, being proceedings in the High Court or the Court of Session or on appeal from a decision in such proceedings, that he has been guilty of adultery with a particular person shall be conclusive of that fact."

Clause 18 is also important and provides for appeal against disciplinary action of the Judicial Committee of the Privy Council. The relevant subsection reads:

"(3) At any time within twenty-eight days of the service of a notification under subsection (1) of this section the person on whom it was served may, in accordance with such rules as His Majesty in Council may by Order provide for the purposes of this section, appeal to His Majesty in Council; and the Judicial Committee Act, 1833, shall apply in relation to the Medical Disciplinary Committee as it applies to such courts as are mentioned in section three of that Act (which provides for the reference to the Judicial Committee of the Privy Council of appeals to His Majesty in Council)."

There are other provisions relating to the restoration of names to the *Medical Register*, and several miscellaneous provisions. Among these there is one relating to the appointment of visitors of medical schools; a clause providing for the publication of new editions of the *British Pharmacopoeia* with amendments from time to time, and there is also a section on registration fees. The maximum fee which may be fixed in the normal case for full registration, which includes a maximum fee of five guineas for provisional registration after passing a final examination, is 11 guineas unless the Privy Council by order vary the maximum.

The short title of the Act will be "The Medical Act, 1950."

IODINE AND GOITRE

INTRODUCTION OF IODIZED SALT

The Medical Research Council recently advised for the prophylaxis of thyroid enlargement and goitre in Great Britain the general use of iodized salt. It recommended the addition of either 1 part of potassium iodide to 100,000 parts of all salt, or 1 part to 40,000 parts of packeted table salt.[1]

These recommendations, first put forward some six years ago, were supported in a leading article[2] which appeared last month in the columns of the *Journal*. The Ministry of Health Standing Committee on Medical and Nutritional Problems endorsed the M.R.C. recommendation, and the Food Standards Committee issued a report last week on the measures necessary to give effect to the recommendation. The Committee was given information by different Government Departments and heard evidence from the British Salt Federation.

Salt Production and Consumption

Less than half the total production of salt in Great Britain is used for food purposes. Of this quantity, about 59% is used in food manufacture for salting, curing, etc., 35% is used in the home, and about 6% in catering establishments. The first recommendation of the M.R.C. would affect all salt which enters into human consumption, but the second would apply only to prepacked salt sold for use in the home. The former alternative is impracticable, and even the iodization of all prepacked salt raises an initial difficulty. Prepacked salt includes stoved vacuum salt, ground open-pan salt, and bar salt (repacked in small pieces as "cut lump"). The addition of iodide to stoved vacuum salt and ground open-pan salt presents no difficulty, but it is technically impossible to iodize bar salt. Prohibition of the sale of all prepacked salt, unless iodized, would therefore bring to an end the retail sale of "cut-lump" salt.

In 1948 the production of salt for use in the home consisted of prepacked free-running salt 65,000 tons, packeted household cooking salt 30,000 tons, and cut-lump salt 24,700 tons. At the present time only 1.6% of the current output of prepacked salt is iodized. The iodization of all prepacked salt would necessitate considerable re-equipment and reorganization in the salt factories. Since the requisite machinery exists, it is estimated that within a year from the issue of an Order manufacturers could iodize that part (i.e., 65,000 tons) of the production of prepacked salt sold as "free-running" table salt—i.e., salt to which small quantities of suitable substances have been added—but that two years would be needed to iodize packeted household cooking salt (which contains no added ingredients to render it free-running). If salt production as between prepacked free-running salt and other salt used in the home remains substantially in the same proportion as in 1948, slightly more than half the population of Great Britain would benefit within the first year from the iodization of prepacked free-running salt and the entire population would benefit by the end of two years.

The M.R.C. recommended that, if packeted table salt only were treated, iodization should be on the basis of 1 part of potassium iodide in 40,000 parts of salt, the permitted limits of variation being between 1 part in 30,000 and 1 part in 50,000. Iodization may be effected by the use of sodium iodide (containing 84.7% iodine) instead of potassium iodide (76.5% iodine), and it would therefore be more convenient to express these limits in terms of iodine; 1 part in 30,000 of potassium iodide is equivalent to 25.5 parts per million of iodine, and 1 part in 50,000 of potassium iodide to 15.3 parts per million of iodine.

Three main methods of incorporating the iodide were described to the Committee: (i) Spraying the salt with a solution of iodide in a mixer, followed by drying. (ii) Spraying the salt on a moving belt system, followed by drying. (iii) Dry-mixing. The iodide is first mixed with about 100 times its weight of salt, and this mixture is then added to the bulk of the salt. It was suggested by the trade representatives that the prescription of a standard method of incorporation of the iodide might be considered. This suggestion has been referred to the Ministry of Food.

Even under the best conditions of storage the loss of iodide is significant, and adverse storage conditions, particularly damp, considerably accelerated the rate of loss. The use of inner and outer wax liners is therefore desirable; without them present packaging materials are unsatisfactory for iodized salt. With the present limited demand for iodized salt its shelf life is estimated to be in the region of two years, but this should be much reduced when iodized salt is in general use. It will, however, be essential to ensure the selling of old stock before new. Even so provision must also be made for losses during storage. On these grounds the trade favoured a range of 15–30 p.p.m. of iodine or, alternatively, 20–35 p.p.m.

Recommendations

After considering these points the Committee took the view that the level of iodization could be more conveniently expressed in terms of iodine and recommended that a standard should permit variation between 15 and 30 parts of iodine per million parts of salt. It is understood that the M.R.C. would raise no objection to this minor modification. The Committee also considered whether the iodization of salt might be brought about by the incorporation of the more stable iodates instead of iodides, but was advised that there is at present no direct evidence that iodate would be assimilated.

The Committee agreed that losses of iodine from prepacked salt due to the absorption of the iodine by the packaging material could be substantially reduced by the use of materials impervious to moisture. Further, the orderly selling of stock would be facilitated by reviving the pre-war practice of date-stamping the packages before they leave the manufacturer or re-packer. The Committee was satisfied that chemical analysis could be relied upon for the enforcement of the standard recommended.

The Committee finally concluded that the following measures would be necessary to implement the recommendations of the Ministry of Health Standing Committee on Medical and Nutritional Problems, endorsing the original recommendations of the Medical Research Council.

(i) *Standard of Composition*: All prepacked free-running salt should, within one year from the date of an Order, contain potassium iodide or sodium iodide in amounts equivalent to not less than 15 and not more than 30 parts of iodine per

[1] M.R.C. Memoranda No. 18, "Thyroid Enlargement and Other Changes Related to the Mineral Content of Drinking Water." H.M. Stationery Office, 1948. Price 9d.
[2] *British Medical Journal*, 1950, **1**, 654.

million parts of salt, and within two years from the date of an Order all other prepacked salt should be similarly treated.

(ii) *Packaging:* To minimize loss of iodine, iodized salt should be packed in containers resistant to the effects of humidity changes. Packages containing iodized salt should be date-stamped before they leave the manufacturer.

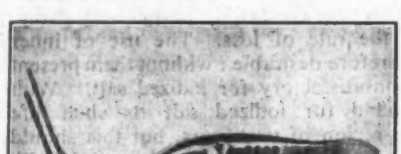
Answering these recommendations in the House of Commons on March 22, the Minister of Food, Mr. Webb, said that the recommendation of the Food Standards Committee would not take effect until June 30, to allow time for any representations to be made to the Committee by the public, the trade, and the medical profession.

Those wishing to make representations should write to Mr. K. R. Allen, Secretary of the Food Standards Committee, at the Offices of the Ministry of Food, Food Standards and Labelling Division, 47, Portman Square, London, W.1.

Preparations and Appliances

A NEW CLAMP FOR PORTOCAVAL ANASTOMOSIS

Mr. FRANCIS E. STOCK, F.R.C.S., professor of surgery, University of Hong Kong, writes: The operation of portocaval anastomosis has been carried out in this clinic on nine occasions through a transthoracic approach after removal of the tenth rib. A direct end-to-side anastomosis is made of the portal vein to the vena cava after division of the portal vein. One of the difficulties of the operation is in controlling the blood flow through the vena cava during the 10 to 15 minutes from the time of ligation and division of the portal vein to the completion of the anastomosis. If the vena cava is completely occluded, as was done in the early cases in the series, the blood pressure falls very considerably during the period of occlusion. V. P. Satinsky (*Ann. Surg.*, 1948, 128, 938) has suggested the use of a Stille kidney clamp to occlude the vena cava partially, but this instrument has seemed to be too clumsy, although a similar clamp was used on several occasions. A small light clamp which would grip the vessel firmly, leave two-thirds of the caval lumen open, and be out of the way of the surgeon's hands seemed to be desirable.



Such a clamp has now been made for me in the engineering workshops of the University of Hong Kong. It is small and light, and can be applied by thumb pressure and fixed in place by a milled nut. The inner surfaces of the blades have a single longitudinal groove which prevents slipping from the vein and yet does not traumatize the vein wall. The clamp has no rubber tubing on the blades. It has been used on the last three cases with complete success. At least two-thirds of the vena cava lumen remains patent through the period of the anastomosis, and the systemic blood pressure does not fall.

Shorter training and a wider field for recruitment are features of altered conditions for the National Hospital Service Reserve in England and Wales announced by the Ministry of Health. Part-time hospital nursing staff, and non-nursing staff, either whole-time or part-time, can now join the Reserve. The only exception is hospital domestic staff. Previously, neither nursing nor non-nursing staff in hospitals or similar institutions could join. Hospital training for nursing auxiliaries has been reduced to 48 hours in six days (whole-time) or 80 hours in nine months (part-time). Compensation to auxiliaries for loss of earning during their hospital training will now be payable whether it is whole-time or part-time provided the period of training is four hours or more. Up to the end of January over 1,800 trained nurses and nursing auxiliaries had joined the Reserve.

Correspondence

Intrathoracic Goitre

SIR,—I abate not one whit of my admiration for the literary erudition and surgical skill of Mr. Geoffrey Keynes as evidenced in his Legg Memorial Lecture (March 18, p. 621), but there are one or two statements which provoke a reply. When discussing the difficult problem set by intrathoracic goitre, he states: "There is always danger lurking in the acquirement of fixed habits of mind. Thus a thoracic surgeon who assumes that all intrathoracic tumours can be suitably removed through a transpleural approach may be for a few moments dismayed. . . . He must then hurriedly try to recollect what he once knew years before about the anatomy of the neck. . . ."

I trust that the average thoracic surgeon would not be so mentally and technically unprepared. Though sometimes regarded as a "specialist" in the derogatory sense of the term, the chest surgeon can claim by training and his practice to be a truly "general" surgeon working over a limited anatomical field. Intrathoracic goitres are fairly commonly met with in thoracic surgery, and in the differential diagnosis of any rounded tumour close to the mediastinum the possibility of abnormally placed thyroid tissue should always be considered. Indeed, some forms of intrathoracic goitre have little or no demonstrable connexion with the neck, and their nature is only finally determined by pathological investigation (the "mediastinal aberrant goitre" of Rives).

Most cases of retrosternal goitre can be removed through the standard neck incision, but, as Mr. Keynes has pointed out, a few cases require splitting of the sternum, which increases the exposure and converts a "blind" into an "open" operation. Whether this is preferable to a transpleural approach in the case of posterior mediastinal tumours is debatable.—I am, etc.,

London, W.1. T. HOLMES SELLORS.

Maternity and the N.H.S.

SIR,—My committee views with grave alarm the article published in your issue of February 18 (p. 392) entitled "Maternity and the National Health Service." Before the Health Service started the B.M.A. issued a statement of the "Fundamental Principles of the Medical Profession in connexion with the National Health Service," of which the second and third are pertinent to the discussion.

2. "The medical profession should remain free to exercise the art and science of medicine according to its traditions, standards and knowledge, the individual doctor retaining full responsibility for the care of the patient, and freedom of judgment, action, speech, and publication, without interference in his professional work."

3. "The citizen should be free to choose or change his or her family doctor, to choose, in consultation with his family doctor, the hospital at which he should be treated, and free to decide whether he avails himself of the public service or obtains independently the medical service he needs."

The committee is very much concerned that a distinguished member of the profession should go so far in his article as to state that his professional brethren are less capable of conducting normal maternity cases than a midwife, and by so doing deny these freedoms to doctor and patient alike, and at the same time gravely prejudicing the harmony that should exist between midwife and general practitioner throughout the country.

The writer of the article states, "The administrative arrangements necessary to regulate the general practitioner's part in the maternity service present considerable difficulty," and further, "It would be unfortunate if in a matter which is confessedly difficult and even delicate we should, through lack of the spirit of conciliation and statesmanship, fail in our effort to reach the aim accepted by us all as the ultimate desideratum—the unbroken continuity and singleness of control of the

woman throughout the whole of her time of pregnancy, labour, and puerperium."

We fail entirely to see any sense of conciliation or statesmanship in the article that is before us where it concerns general practitioners, who incidentally far outnumber the specialists and probably conduct far more maternity cases. It appears to us, representing the 1,550 general practitioners in Middlesex, that the ultimate aim of us all, to help the patient in the best way possible, is ill served by one section of the profession decrying the capabilities of another section.—I am, etc.,

London, W.C.1. R. L. RIDGE,
Chairman, Middlesex Local Medical Committee.

SIR,—Your issue of February 18 contains much food for thought for those interested in obstetric practice in this country. Professor James Young (p. 392) does a great service in pleading with such vigour for an integration of purpose and effort. Not everybody will agree, however, with his lavish idolizing of midwives. To my mind it does not make sense to talk of "degrading the midwife to the status of a maternity nurse," because after all a midwife is a nurse and not some strange hybrid on a different plane. The late Joseph de Lee, who is recognized as one of the greatest obstetricians this world has seen, stated quite emphatically that "every labour should have two physicians if possible."[1] This, of course, is an ideal which cannot be realized in this country at the moment except in a very few favoured cases. It is very important, however, not to reject an ideal simply because it cannot be fulfilled.

Of course those people who maintain that normal midwifery is the special province of midwives, and should remain so for all time, are the victims of faulty reasoning. Parturition, they say, is a "natural" process; therefore leave it to "nature" and all will be well. It were as if "nature" were an all-wise, perfect, and sufficient demigod. The truth of the matter is that to sustain a compound fracture of the femur, to develop peritonitis, and to have one's shoulder blown off in battle are also natural events in that they occur with great frequency in the realm of nature. Truly nature, as opposed to an individual's idealized concept of nature, is most imperfect and very often is quite cruel. Parturition is a process which very often goes wrong and very often manifests the imperfection of nature. The attitude of mind of the obstetrician therefore should not be one of adoring passivity but should be akin to that of a general in command of an army in the field. The good obstetrician has to be a master of a strategy of a special sort and able to perfect imperfect parturition by the successful imposition of his will; and in making this assertion the last thing I have in mind, needless to say, is the "meddlesome midwifery which has cost thousands of valuable lives."[2] The perfection of parturition which I have referred to can be accomplished only by one who has had a full medical training.

Another important point to notice is this. While it is true to maintain that a high maternal and foetal mortality rate points to bad midwifery, the converse is not necessarily true. Good obstetric practice entails more than low mortality and morbidity rates. I myself know two large maternity hospitals where the mortality rates are very low but where I cannot describe the practice of midwifery as excellent. As I see it, it is mainly because British obstetricians have thought too exclusively in terms of mortality rates that their plans for a national maternity service have not met wider acceptance. Their plans have been good so far as they went, but they have never gone far enough. The supercilious attitude adopted by many obstetricians to the subject of analgesia in childbirth is just one example of the frame of mind to which I am trying to draw attention. Even on reading Professor Young's paper one feels that he is far more concerned with "the status of the midwife" than with the comfort of his parturients.

It is disappointing to see so much criticism, to a large extent by innuendo, of general practitioners in Professor Young's paper. As one who has seen a good cross-section of midwifery in this country I can confidently affirm that neither section of our profession is in a position to throw stones at the other.

Finally, in the same issue of the *Journal*, Professor Alexander Kennedy deals with some very important matters in his paper entitled "The Psychology of the Surgical Patient" (p. 396). It is my considered opinion that obstetrics will gain enormously when a similar study is made of the psychology of the obstetric patient.—I am, etc.,

JAMES ROSS.

REFERENCES

1 *Principles and Practice of Obstetrics*, 1943, Philadelphia, p. 243.
2 Ibid., p. 267.

SIR,—A further article on the maternity service by Dr. D. W. James has now appeared in your *Journal* (March 11, p. 598), which, following on that of Professor James Young (February 18, p. 392), shows only too clearly the policy of our senior colleagues in this particular branch of medicine. Having shown that the greatest single advance in the reduction of maternal mortality was the discovery and use of chemotherapeutic agents, he concludes his article by saying, "If there is an increase in mortality [maternal] then general-practitioner midwifery is finished for all time." Why is the G.P. selected as the scapegoat for any possible future rise in the maternal mortality rate when it is clear that two other persons are equally involved—e.g., the midwife and the specialist? To quote examples of bad G.P.s is as useless as it is odious, and it would not be difficult for G.P.s to retaliate in kind. Surely, if it is thought that the G.P. is not fit to undertake midwifery, this is a matter for a searching examination of our present teaching. To make a man pursue a certain prescribed course, sit and pass an examination, and finally give him a licence to practise, then to withhold that right on the grounds that he has no special knowledge is nothing short of chicanery.

But I am concerned with much wider issues. What is happening in obstetrics to-day can be happening in, say, children's diseases to-morrow. Pushed to its logical conclusion, the newly qualified doctor could find himself precluded from practising any branch of medicine for the reason that he has no special experience. The fear that this may happen is only increased when one considers the alarming growth of quasi-specialties and their concomitant diplomas (e.g., D.C.H., D.A., etc.) which has taken place in the last few years. The role of general practitioner sorting-clerk looms amazingly near, and is not such a figment of the imagination as many would have us think. Something must be done to stop this dismemberment of the general practitioner.

It is pertinent to note that these articles, which so closely affect the G.P.'s future, are not ministerial in origin. We are gradually being degraded by our own colleagues, those in high places who have access to the official ear. (This probably throws some light on the amazing debacle of the profession after the second plebiscite.) It is now up to these same colleagues to see that this policy is reversed and that the general practitioner gets a square deal.—I am, etc.,

High Wycombe. W. YOUNG.

SIR,—The reflections upon the emergency maternity service by Dr. D. W. James (*Journal*, March 11, p. 598) are so startling that they might have come from the pen of Dr. Cronin. Who will champion the cause of the general practitioner? Nay, shortly, who will become a general practitioner—apparently the most incompetent member of the profession?—I am, etc.,

Glasgow. J. E. KENNEDY.

An Appendicular Faecolith

SIR,—Mr. Eric Coldrey (March 18, p. 673) is quite right when he says that appendix concretions opaque to *x* rays have received scant recognition in the standard textbooks. I came across a striking example of this condition some years ago and published a brief note in the *Journal* (December 20, 1930, p. 1041). If Mr. Coldrey turns it up he will find a number of references to the literature on the subject. In the *Journal* of July 27, 1907 (p. 199), Dr. O. T. Williams, of Liverpool, wrote an account of the growth of the calculi *in situ* by a process of saponification.—I am, etc.,

Liverpool. CHARLES WELLS.

Acute Laryngo-tracheo-bronchitis

SIR,—With reference to Captain John Z. Garson's article (March 11, p. 578), we feel that there are certain points to which attention should be drawn. Several cases in young children have been met with in this part of the country, and only in the mildest has it proved safe to rely on "aureomycin" alone. Patients have died where this has been the sole form of therapy, death being due to unrelieved mechanical obstruction. In all but the mildest cases, tracheotomy followed by repeated bronchoscopic suction and steam inhalations are nearly always called for, and recently we successfully treated a very severe case by this method without employing the newer antibiotics.

Treatment must be instituted at the earliest moment, and from our experience and that of others the ideal treatment in most cases would seem to be tracheotomy, repeated bronchoscopic suction (which may be necessary three or four times a day), combined with aureomycin to attack the virus and penicillin and the sulphonamides to combat secondary infection. In view of the stickiness of the exudate it is also very important that the child should be nursed in a steamy atmosphere, our experience being that an oxygen tent by itself not only does not help but has the effect of drying the secretions, causing further obstruction and extreme restlessness, as it did in Captain Garson's case.—We are, etc.,

Worthing. IVOR H. C. BALFOUR.
PETER C. RUSHTON.

SIR,—Captain J. Z. Garson's article (March 11, p. 578) stresses well the alarming rapidity with which acute laryngo-tracheo-bronchitis may progress to death unless checked—an experience all too unhappily remembered by many paediatricians. This disease appears commoner in America than in the British Isles—at any rate in the Middle West and East—and quite recently I was able to observe or collect details on the course of some twelve cases. There are two points I would like to mention in connexion with Captain Garson's account.

1. It seems that a variety of organisms, profusely growing, can be cultured in any series of cases (two, I recall, gave pure growth of *Haemophilus influenzae* from laryngeal swabs). Captain Garson is right to stress the penicillin-resistant staphylococcus, but other organisms may also be resistant and cause the disease, while the virus aetiology theory is very plausible and must be kept in mind. Therefore I am unhappy when he suggests that "owing to the rapid and fatal course, the first line of treatment must be with one of the newer antibiotics." This is a rapid and dangerous disease, and one is not sure what organism one is fighting. It would therefore seem rational, even if heroic, to administer full doses of penicillin, sulphonamide, and streptomycin or "aureomycin" all together. This in fact was done in the later cases which I mentioned, with significantly better results. (In passing, Captain Garson does not welcome streptomycin "because of side-effects." These are minimal, especially with newer forms of streptomycin—e.g., dihydrostreptomycin—and of no consequence when one may be saving life.)

2. The most likely cause of rapid death in these cases is the overwhelming toxaemia. Very often the case reaches the doctor too late. Even if it comes early, when the diagnosis is not in doubt, energetic therapy must be started at once (without waiting for culture results) if the child does not improve in general condition quickly after mechanical obstruction to breathing has been relieved.—I am, etc.,

London, W.C.1. FRANK FALKNER.

Speech Disorders in Childhood

SIR,—The article on this subject by Miss M. Morley and Drs. D. Court and H. Miller (March 11, p. 574) will be read by many doctors, including school medical officers. As one of the latter I have been most interested to find how greatly their outlook of working in a hospital and university seems to differ from those working in the schools. For instance, the authors found that the percentage distribution was: stammering 40, dyslalia 26, etc. In my own area my speech therapist colleagues find a very different picture—namely, stammering about 31, dyslalia 61, etc. Age, of course, makes a difference, some children growing out of their speech defects as promised so often by the family doctor, but in the schools speech therapists seem to find considerably more dyslalias than stammers. The defect may be a great handicap in linguistic subjects.

Receptive Difficulties.—Case 1 is given as illustrative of a deaf child with severe speech difficulty, but, although the deafness was apparently severe, consideration for a school for the deaf is postponed by the authors until the child is 5 years of age. In such a case the question of the school for the deaf should have been considered from the age of 2 years as is required by the Education Act of 1944. Opinions may differ on whether a child of under 3 should be transferred to a residential school at such a tender age, but the matter should have active consideration from the earliest years. In my own area we have been distressed to find that difficulty of getting trained staff for our day school for the deaf has occasionally forced us to defer admission of deaf children until 4 or 5 years of age.

Cleft Palate.—It is surprising to find that the authors make no reference to non-closure of the palatopharyngeal sphincter resulting from shortness or immobility of the soft palate so often left after apparently successful closure of cleft palate. Miss Morley herself lays considerable stress on this factor in her book *Cleft Palate and Speech.* It is surely of much greater importance than the small cleft in the hard palate which may close spontaneously or be occluded by a dental plate or even make little difference to speech whether closed or not. Operative treatment may be difficult, calling for the highly technical attention of a plastic surgeon, but I would suggest that he should invariably be consulted when any deficiency in the soft palate is suspected.

Stammering.—It is acknowledged by the authors that some stammering may be due to psychological factors, but they leave the impression that they consider that it is the "more severe or intransigent" cases which should be referred to the psychiatrist or physician. Is this fair on either the child or the psychiatrist? Many slight stammers are due to psychological factors which should be dealt with by the psychiatrist and not by the speech therapist. It may be impracticable to refer every case of stammering to the physician or to the psychiatrist, but the speech therapist should always be on the look-out for such cases, and should be afforded every opportunity of referring suitable cases to the physician and the psychiatrist before treatment is started, and should not have to wait until the case becomes "intransigent."

Speech Disorders in Mentally Retarded Children.—The authors stress the danger of diagnosing mental defect too hastily, but they say that "a simple inquiry for the 'milestones,' the age of sitting up, walking . . . will often enable a provisional assessment (of mental deficiency) to be reached." Anyone who has examined a number of maladjusted mentally deficient or educationally subnormal children knows how little reliance can be placed on these data. As suggested by the authors, there are many factors other than mental defect which may cause displacement of these milestones, and it is most dangerous to place any reliance on them even in attempting a provisional assessment. The more intelligent parent, during an interview which is often embarrassing to her, finds great difficulty in giving accurate information on such points, whereas the unintelligent parent of an obviously imbecile child will cheerfully give fantastically early ages—so much so that I have come to look upon these ages not as "milestones" but as "movable feasts."

Surprise, too, may be expressed that the authors pay no tribute to the value of contact with other children in nursery classes or even in 5-year-old classes for certain cases of speech defect, especially when a child has been isolated from others by being an only child or by hospitalization. Although teachers in ordinary schools cannot be expected to undertake remedial speech therapy they may be the first to notice a speech defect which a child may often ingeniously conceal when being examined by a doctor, and with a sympathetic understanding of the needs of the child and the aims of the speech therapist they can often help very considerably when a child is under treatment.—I am, etc.,

Nottingham. A. A. E. NEWTH.

Adrenal Cortical Tumours

SIR,—Dr. George Lumb (March 11, p. 582), reporting two cases of large adrenal cortical tumours which showed no hormonal activity, says : " Fuchsinophil staining by Broster and Vines's (1933) method gave for the most part negative results, although occasional granules scattered through the cells of the tumours took up the red stain feebly." This wording suggests uncertainty about the results of the method.

Some time ago I tried this method on an adrenal gland, not a tumour, from a case of virilism, so that a positive result was to be expected. However, the results obtained by the method described by Broster and Vines[1] were indefinite; I found it impossible to reproduce the appearances shown in their illustrations and in a section, in the possession of one of my colleagues, which Professor Vines was believed to have stained. In my preparations red-staining granules were seen in the cells of the zona reticulata, but they stained neither very strongly nor much more strongly than many other structures. Moreover, the cells of the cortex generally stained red or pink, instead of the blue shade shown in the pictures and sections mentioned.

After many experiments I found it was possible to get the desired results by " post-chroming " for 24–48 hours at 37° C., staining in ponceau-fuchsin for 5–10 minutes, differentiating as described by Broster and Vines, and then prolonging the time in aniline blue until the cortical cells lost their residual pink or red and became blue or purplish. This might require 30 minutes or more. In this way strongly fuchsinophil granules could be demonstrated in abundance in many of the cells of the zona reticulata, but few or none in the corresponding cells of a number of control cases.

Subsequently Dr. Doniach, of the British Postgraduate Medical School, kindly drew my attention to the " Picro-Mallory " methods described by McFarlane (1944).[2] I experimented with this on sections from the case previously worked on, from another adrenal in a case of virilism, from a virilizing adrenal tumour, and from controls, and eventually worked out the following modification, for paraffin sections of formol-fixed tissue.

Post-chrome for 12–24 hours at 37° C. (This is not essential but gives brighter results and makes the subsequent differentiations easier to control.) Lugol's iodine 5 minutes, running water till the sections are fully decolorized. Weigert's haematoxylin 15 minutes; wash in tap water. Differentiate in picro-orange until only the nuclei are stained; wash in tap water until only red corpuscles are yellow. Stain in ponceau-acid fuchsin 20 minutes; differentiate in " red differentiator " 10–20 minutes (to ensure that only truly fuchsinophil elements remain red). Stain in aniline blue 15–30 minutes or more as required (this will give a blue colour to many structures which would ordinarily remain red, but some structures such as fibrin and the fuchsinophil granules under discussion will still be a definite red). Differentiate in " blue differentiator," so that structures overstained in the preceding stage become pink or mauve —30 seconds to 5 minutes (this produces a more " natural " appearance in such structures as blood vessels). Rinse in distilled water, dehydrate, mount in Canada balsam.

In my hands this method demonstrates fuchsinophil granules in cells of the zona reticulata in the adrenal glands mentioned and in scattered cells of the adrenal tumour mentioned, while in most normal adrenals such granules are absent or comparatively scanty. (In one control the fuchsinophil cells were too numerous to be called " scanty," though less numerous than in the cases of virilism.)

Staining and differentiation, especially the latter, must be controlled under the microscope. Moreover, examination of the stained section should be done with a 1/6 in. or a 1/12 in. objective, since cells of the zona reticulata in normal adrenals may contain granules staining orange or blue, or even green, the orange ones being sometimes quite numerous. It is important to study the staining of the section as a whole; indeed, I think that as one gains experience of the stain and the tissue under investigation one learns to depend less on minor variations between different preparations and more on differences between parts of single preparations.

It seems probable that different workers will have to find out by experiment how to produce the desired results, for it is a commonplace that different samples of these stains behave in different ways. This may perhaps account for the difficulty encountered with Broster and Vines's original method. A converse difficulty is that variations of technique give such variations in the results with the same stains. For example, the number of fuchsinophil granules in a given cell diminishes as the length of staining in aniline blue increases, though a few maintain an unimpaired redness after 45 minutes. The aniline blue seems at first merely to cover up the red stain, for the red can be " unmasked " by " blue differentiator " ; but if the aniline blue is allowed to act for an hour or more it replaces the red, and then " blue differentiator " merely lightens the blue. I once left a section of kidney in aniline blue for three days ; everything went blue except for some curious bright red bodies in a few tubular cells. The question arises, " When is a structure fuchsinophil ? And if it is, what does it signify ? " I think the answer can come only from critical cytochemical study, and it will probably be given in more precise and meaningful terms.—I am, etc.,

London, W.2. R. R. WILSON.

REFERENCES

[1] *The Adrenal Cortex*, 1933, London.
[2] *Stain Technology*, 1944, 19, 29.

Anaesthesia for Fenestration Operation

SIR,—In the correspondence on anaesthesia for the fenestration operation, Dr. Rex Binning (March 11, p. 608) recommends as premedication in adults, nembutal 6 g., omnopon gr. ¼, and scopolamine gr. 1/150. I would suggest that either " g." was a misprint for " gr." or that this combination is a dangerous overdosage.—I am, etc.,

St. Albans, Herts. C. LANGTON HEWER.

⁂ Dr. Langton Hewer's first suggestion is correct.—ED., *B.M.J.*

SIR,—The factors which have to be considered when choosing an anaesthetic technique for this operation appear to indicate the use of thiopentone throughout the operation. Oral intubation may be carried out under 0.75 to 1.0 g. of thiopentone combined with a 10% cocaine spray to the larynx. A large Magill tube, size 9 or 10, is passed and connected to a Boyle's machine delivering 30–40% oxygen in a gas-oxygen mixture. Anaesthesia is continued by means of a thiopentone drip. Two grammes of thiopentone in 400 ml. of sterile water is a suitable dilution to provide an easily controlled anaesthesia, the depth of which is gauged by the respiratory excursion.

This method provides the desirable conditions for the fenestration operation which have been mentioned in earlier letters—i.e., quiet respiration with a slight reduction of blood pressure to minimize oozing. A good airway is assured. Diathermy or adrenaline may be used. No other cause for vomiting is added to the labyrinthine disturbances which may follow the operation. Depth of anaesthesia can be maintained at an even level which is adequate for the operation and not deep enough to cause a build-up of CO_2, resulting in unnecessary capillary oozing.

We make no claim to originality for this technique, which has been used for Mr. J. A. Harpman's cases at Warwick Hospital for the past two years.—We are, etc.,

Warwick. D. R. RIGG.
R. P. PARKER.

Sadism on the Screen

SIR,—I am grateful to Mr. A. R. Thornton for his letter (March 18, p. 673), but cannot agree that the facts he adduces in any way invalidate my own. I did not say, nor do I believe, that the cinema is the sole cause of crime. The work of Healy, Alexander, Menninger, Wertham, East, and others shows that such an idea is untenable. Moreover I agree with Mr. Thornton on the tremendous importance of proper home life, as I have stated elsewhere.

The child, most psychiatrists will agree, develops sadistic feeling early in its development but " works through " or resolves this by contact with its environment—mainly its parents. It introjects, or moulds itself upon, its mother and father and obtains its conscious and unconscious ideas of right and wrong from them. However, if through war or some other cause its home life is spoiled it absorbs its ideas from elsewhere —for example, from the cinema. A child gets rid of much of its sadism in play, but after puberty it realizes that adults do not indulge in fantasy games and cruelty is particularly abhorrent to the grown-up. If, however, it finds itself in a *milieu*

where sadism is approved the resolution of its cruel impulses will be delayed and it will remain sadistic.

The sadistic films of the last ten years have done infinite harm in this way. It is just because of the broken homes that the cinema should avoid anything in the suggestion of vicious cruelty. Adults often insist that because they feel no ill-effect from a sadistic film then such a thing must be harmless; but adults derive little ill-effect from a cocktail or a glass of spirits, though one would not give such drinks to children.

Mr. Thornton says that films are not sadistic, yet will he deny that the film critics of such responsible papers as the *Daily Telegraph*, the *Sunday Times* and similar serious journals have constantly complained of the exhibition of needless cruelty on the screen? That sadism was present during the war, if not so marked as now, is shown by the fact that I saw a film called "The Glass Key" in 1943 and this was unnecessarily brutal.

Mr. Thornton asks for information regarding objectional methods of film advertisement. Well, here it is. About three weeks ago London was plastered with posters advertising a film called "White Heat," depicting James Cagney bashing someone on the head with a revolver butt while a girl stood watching. A fortnight ago another film called "Borderline" was advertised with a man holding a smoking revolver with a girl behind him: the delights of this were recorded as "Three murders behind and two hundred miles to go." I suppose he will not regard these as examples of "apparent cruelty" or "brutality," but, if they are not, what is? A recent issue of the *Picturegoer* states that an actor, "who obviously believes in getting into pictures the hard way, was paid £20 for enduring two days' 'flogging.' Although the actor whose job it was to mete out the punishment was ordered to make it as painless as possible, there were several weals, real or imaginary, on the 'prisoner's' back when the close-ups had been shot."

I have read the Hays code and agree that the cinema industry should control itself, but why does it not do so? Why does it object to trivialities like the authentic dresses in "The Wicked Lady," and pass bashings on the head and brutal fights? Surely it is grandmotherly to suppress normal sex and allow adolescent sadism? I read *The Young Delinquent* in 1927, but cannot see what relation this book has to the present wave of sadistic films. What Burt wrote then has nothing to do with present conditions.

I would assure Mr. Thornton that I am an ardent cinema-goer and can enjoy thrillers with anyone—who can forget the terrific tension of "The Window"?—but we need more films like "Bicycle Thieves." Incidentally, I have read this was banned in America by the Hays Office. Films which show the misery produced by crime and not the glorification of the gunman. We must rid ourselves of the boring sadistic matter which I insist is doing grave harm to young people.—I am, etc.,

London, W.1. CLIFFORD ALLEN.

A Useful Hobby

SIR,—When retiring twelve years ago from general practice, golf, car, and gardening happily filled the first few years. Then illness came along and restricted my getting about and so stranded me for something interesting to do. By happy chance a braille letter came and, as it was all double Dutch to me, set me thinking about it and making inquiries. These resulted in my taking up a free correspondence course, gaining a certificate of efficiency, and becoming useful in transcribing into braille articles, small books for blind school-children in Africa, etc.

There is a small circle of deaf-blind people who keep me well occupied doing the articles they require and such things as broadcast sermons, "the parson calls." Helping with the birth of a novel—without getting up at 2 a.m.—had a thrill of its own by transcribing a blind author's braille. Teaching braille has brought interesting contacts, and I felt sorry for a brave lady of 82 who found the accuracy required too much for her. Unlike cross-word puzzles, there is the feeling of helping the less fortunate, and without having to go out of the house to do so. There is plenty of room in the ranks of braillists and plenty of work for them to do.—I am, etc.,

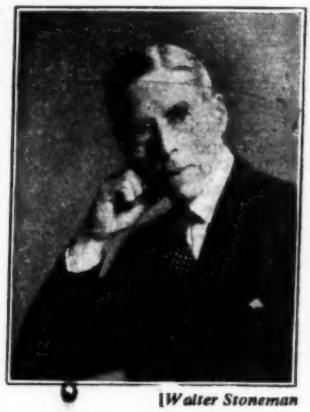
Bradford. ROBERT CRAWFORD.

Obituary

F. W. TWORT, M.R.C.S., F.R.S.

Dr. F. W. Twort, the discoverer of a lytic phenomenon now known to be due to the bacteriophage, died at his home in Camberley on March 20, at the age of 72.

Frederick William Twort was the son of Dr. W. H. Twort, and received his medical education at St. Thomas's Hospital, where he qualified in 1900. His interests were early directed to bacteriology. Until 1902 he was assistant superintendent of the clinical laboratory at St. Thomas's, and thereafter, until 1909, assistant bacteriologist to the London Hospital. In that year he was appointed superintendent of the Brown Animal Sanatory Institution in the Wandsworth Road, London. There he remained, except for an interval of military service in the first world war, until his laboratories were destroyed during the blitz on South London in 1944. In 1908 he received the Rogers Prize from the University of London, and many years later the title of "Professor of Bacteriology in the University of London" was conferred on him in respect of his appointment at the Brown Institution, which he had directed for so long.



[*Walter Stoneman*

Twort's early work involved the discovery of an essential growth factor for Johne's bacillus as a result of which the organism could be cultivated and a vaccine prepared. His observations were summarized in an important monograph on Johne's disease published in 1913; they paved the way for the many investigations which have since been made on the nutritional requirements of bacteria. The work by which Twort will always be remembered was a by-product of his observations on the purification of vaccinia virus. At the time these observations were published, during a most critical period of the 1914–18 war, they passed almost unnoticed. Few realized in 1915 that the inconspicuous title, "An investigation on the nature of ultra-microscopic viruses," headed an article which showed that an entirely new group of parasitic organisms had been discovered. During 1916 Twort, as a captain in the R.A.M.C., was in charge of the Base Laboratory at Salonika. Here he did much to counteract the then firmly held dogma that the prevailing dysentery was amoebic in character. During the enforced immobilization imposed by malaria on the Allied Armies in this theatre Twort lectured to groups of medical officers on his new lytic phenomenon. It is perhaps more than a coincidence that Felix d'Herelle served for a time in the French forces which were likewise immobilized at this base; d'Herelle's first paper on the bacteriophage was published in 1917. Twort returned to his studies at the Brown Institution in 1919, and till 1936 his meagre salary was augmented by a grant from the Medical Research Council. He was elected F.R.S. in 1929.

Twort was one of those erratic geniuses who find life far from congenial in our planned and regimented age, when research has become so costly that it can no longer be financed by the private citizen. He would perhaps have been a happier man had he flourished in the reign of

Charles II, in the earliest days of the Royal Society. Even so it is doubtful whether the Petition of Right which he attempted to bring against the Medical Research Council in 1936 would have had any greater success in that age than in our own. Apart from his bacteriological work Twort was intensely interested in many widely scattered fields of study. He married Dorothy Banister, and to her and his four children, and his brother, the sincere sympathies of those who knew and respected Twort and admired his work will be offered.

A. H. PROCTOR, D.S.O., M.D., M.S., F.R.C.S.Ed.

Colonel A. H. Proctor, who was dean of the British Postgraduate Medical School for the first ten years of its existence, died on March 23 at Hexham.

Alfred Henry Proctor graduated M.B., B.S. at the University of Durham in 1902. His medical career was interrupted by the South African war, in which he served as a trooper. He went on to take the M.S. in 1904, and gained a gold medal for his M.D. thesis a year later. Soon after completing the usual house appointments he joined the Indian Medical Service and began a notable career which culminated with his appointment as Inspector-General of Civil Hospitals in the United Provinces. He was honorary surgeon to the Viceroy from 1933 until his retirement on being appointed dean of the newly created British Postgraduate Medical School. During his long service in the I.M.S. he never lost his interest in surgery, and when home on leave he always visited the wards and operating theatres of the Royal Infirmary in Newcastle. In one of these interludes he also did some postgraduate work in Edinburgh, and took the Fellowship of the Edinburgh College in 1923. Colonel Proctor served on the Naval and Military Committee of the British Medical Association, later the Armed Forces Committee, and on the Central Medical War Committee. Apart from his valuable work on these and other central committees he was a member of Council in 1935 and from 1944 to 1947. On more than one occasion his profound knowledge of Indian affairs was of the greatest help to the Council in its deliberations.

Professor G. Grey Turner writes: When I was appointed professor of surgery at the British Postgraduate Medical School in London Proctor was serving in India. Almost at once the deanship became vacant and Proctor became an applicant, coming from India for interview at his own expense. He was appointed to the post and soon took up his duties. That was in 1934 when things were in a very fluid state, so that he was at once confronted with many problems of organization and development. Fortunately in administrative posts in India he had become familiar with organization, planning, estimating finance, and medical administration, and his long I.M.S. experience stood him in good stead. Those of us on the staff at once found him a great help, and from the outset his calm, deliberate, unperturbed manner was a tremendous asset, especially when tempers became frayed and small bothers crowded upon us. Another of his great qualities was his integrity and his high sense of duty. He never tried to impose any discipline that he did not himself observe. At that time Sir Austen Chamberlain was chairman of the governing body, and I feel sure was at once attracted by the qualities of the new dean. He found in him a person he could trust and who was co-operative and helpful. This confidence was continued when Sir Austen died and was succeeded by Sir John Calcutt, for the chairman and the dean soon became fast friends. The same happy relations existed between the dean and Professor George E. Gask, who in those early years was chairman of the school council.

We were a very happily assorted body. Of course there were difficult days with many problems and conflicting interests and ideas, for we had to start from scratch, and the school and the hospital were in the hands of two separate bodies. In these circumstances patience and forbearance were essential, but Proctor was richly endowed with these qualities. He was always easily accessible to the staff, and no one hesitated to consult him. From a senior staff member and one of his oldest friends this statement may seem biased, but members of the junior staff frequently told me how helpful they found these interviews and how readily they were granted. His office staff and the technicians were devoted to Colonel Proctor, and always found him a considerate administrator. Proctor was really interested in the nature, the scope, and the development of postgraduate training and gave much thought to the subject. Not long before the recent war he went to Germany on behalf of the school to find out what was being done in postgraduate education, and what he had to report on his return was not a little disturbing. When the war finally broke out it was obvious that Proctor was restless and itching to be in the fray, but he stuck to the school and carried on. There were many who thought the school should close down, but Proctor believed it could fulfil a mission, and his faith and drive enabled it to carry on and to play a useful part.

Proctor always had the attributes of a clinician, and it was to that side of medicine that he leaned. During the war his clinical training stood us in good stead, for he helped in the hospital work and undertook a certain amount of operating. He also took his share of Home Guard duties, and I believe he rather enjoyed the experience. He was fond of the microscope and inclined to research, and he often started some piece of work as a recreation. In 1944 Proctor relinquished his duties at the school on attaining the age limit of 65. He was made emeritus dean, and his retirement was marked by a presentation from the staff, the council, and the governing body, as well as from the office staff and the technicians. He was very soon in harness again as medical superintendent in charge of the E.M.S. hospital at Southport. There he undertook a certain amount of clinical work which he enjoyed, and he was particularly useful to the junior members of his staff, stimulating and encouraging them in many ways.

His principal relaxation was fishing and the life in the open air which it entailed, and he loved to get up to the rivers of his own Northumberland or to try for a salmon in Aberdeenshire. Proctor only retired from his post at Southport two years ago, and he went to live in Hexham in his home county. There he had secured a nice house and garden, and it is very sad that he was not spared to enjoy a few years of rest and contentment.

V. B. G.-A. writes: The passing of Alf Proctor severs a precious link forged 40 years ago when he, J. D. S., and I were resident officers at the Medical College, Calcutta. He had joined us straight from the troubles in China. Indeed, like all north-countrymen he loved wars, for in his student days he served for three years in the South African Campaign, and I remember how often he used to regale us with bitterly amusing stories of his veldt experiences. Proctor was the typical Geordie, deliberate in speech and rugged in his adherence to facts and detail, the latter showing itself particularly in a slow, meticulous surgical technique which was always good. In 1914 we all went to France, he to the Gurkha Rifles, where for 18 months he did sterling first-aid work in the front-line trenches of those days. When later

he received a D.S.O., after the Battle of Sheik Saad and the advance on Bagdad, everyone was delighted. On his return to India he filled various clinical appointments most excellently, and particularly well that at the Presidency General Hospital, where his flair for surgical team organization first showed itself, and for which the European community and the nursing staff were deeply grateful. Eventually he was promoted to be Inspector-General of Civil Hospitals, where his great energy, clear thinking, and organizing capacity had full scope. His character was dour and doughty, not making friends easily, and despising intrigue and flattery. It was these traits, perhaps, that prevented him from receiving those usual Indian honours which he so fully earned. In his quiet way he loved India and the Indian, taking a particular interest in their bodily health, for he was himself a big athletic man and so it gave him much distress to see good brains housed in bodies that were weak. Knowing him as I did, I think it was a certain sense of frustration that urged him to accept the first deanship of the British Postgraduate Medical School, a job that he held for ten years and for which by his career and training he was so eminently fitted. I feel sure that all those who knew Alf Proctor will wish to convey their deepest sympathy to his wife and two sons, one of whom is in the profession.

S. VERE PEARSON, M.D., M.R.C.P.

Dr. Vere Pearson, who was well known for so many years as superintendent of the Mundesley Sanatorium, from which he retired only a year ago, died in Kingston, Jamaica, on March 19, at the age of 75.

Sidney Vere Pearson was the son of the Rev. S. Pearson, a Liverpool Congregational minister, and was educated at Manchester Grammar School, Highgate School, Emmanuel College, Cambridge, and St. George's Hospital Medical School. He rowed in the Cambridge eight in the Boat Race of 1898, though his friends thought he should have been selected much earlier. He took the conjoint diploma in 1901, and the M.R.C.P. in 1902. Also in 1901 he graduated M.B., B.Ch., proceeding M.D. in 1913. After being a house-physician at St. George's and at the Brompton Hospital, and later resident medical officer at the Shadwell Children's Hospital, he became medical registrar to St. George's Hospital and assistant physician at Shadwell. All seemed set fair for a successful career as a London consultant, and Vere Pearson was already sharing consulting-rooms with T. C. (later Sir Crisp) English, when in 1904 a sudden haemoptysis upset all his plans. He was advised to place himself under the care of Otto Walther at Nordrach, and after many months in the Black Forest he eventually made a good recovery. For a time he toyed with the idea of resuming his original ambitions, but finally decided not to do so, but to devote himself to the care of the tuberculous. In making this decision Vere Pearson was undoubtedly influenced by Dr. Otto Walther, whose colourful personality and great knowledge had a lifelong effect upon him.

In 1905 Vere Pearson followed Noel Bardswell as physician to the Mundesley Sanatorium, where he reigned, a benevolent autocrat, for forty-four years. Before long he had built Mundesley up to one of the most renowned private sanatoria in the world, and he himself soon became, and remained, one of the outstanding figures in the world of tuberculosis. His name first became associated with collapse therapy in 1911 when he published, with A. de W. Snowden and Claude Lillingston, "A Case of Artificial Pneumothorax," the first case to be induced in England. In 1912 he was hunting high and low to find a surgeon willing to undertake thoracoplastic operations; and it was always a great regret that he did not then meet Morriston Davies, who at that time was thinking along the same lines. In 1921 Vere Pearson introduced thoracoscopy into this country, and he was also a pioneer in the cauterization of adhesions.

Of his many contributions to the literature of tuberculosis, his first was an article on "Temperature as a Guide to Prognosis and Treatment in Tuberculosis," the careful study of which is as rewarding to-day as it was some forty years ago. In another paper, "The Pathogenesis of Pulmonary Cavities," published in 1928, he described experiments which showed the air pressures in tuberculous cavities to be above atmospheric pressure. The significance of this discovery was not grasped in this country, and it was left to Caryllos in America to acknowledge that it was Pearson who first conceived the modern idea of "tension cavities." Throughout his life Vere Pearson was interested in the psychology of the tuberculous, and both preached and practised the doctrine of treating the whole patient. Many of his patients remember with deep gratitude the ungrudged hours he spent discussing their personal problems. He was indeed a physician.

Medicine, however, was only one of his numerous interests, which ranged from the Independent Labour Party, town and country planning, and "Henry Georgism" down to—as was jestingly said—"everything beginning with P"—for example, pigs, poultry, paintings, population, peas (sweet). His autobiography, *Men, Medicine and Myself*, published in 1946, unwittingly presents the self-portrait of a near-genius with a zest and a curiosity which were boundless. In student days he attracted the affectionate sobriquet of SeVere Pearson, no doubt because severity of any sort was the exact opposite of his mentality. He was immensely tall, with a slightly melancholy expression when at rest, which was at once dispelled when his interest was aroused. Intense honesty, kindliness, and sympathy were among his leading characteristics. He joined the B.M.A. soon after qualifying, and was president of the Section of Tuberculosis in 1927. He married Miss May Elizabeth Earl, of Norwich, who survives him with their son and daughter.

W. P. writes: For nearly 20 years I have been privileged to feel the greatness and generosity which were behind all that Vere Pearson said and did—the vision which made him introduce collapse therapy into this country some 39 years ago, the bold spirit of naturalistic inquiry which led him to the discovery of the tension-cavity, the countless innovations which he designed in order to make his most intimate friends, his patients, more comfortable, and the burning sense of justice and fairness which inspired his views as citizen and economist. His autobiography, *Man, Medicine, and Myself*, though partly anecdotal in character, is a masterpiece of general medical literature and at the same time testifies to his modesty, for in it he gives to others much of the credit which is due to him. Pearson's work will live—in his institution, in his ideas, in medical history, and in his literary remains and associations.

A. H. EVANS, O.B.E., M.D., M.S., F.R.C.S.

Mr. Arthur Henry Evans, who died at his home in Forest Green, Surrey, on March 20, at the age of 78, entered as a student at the Westminster Hospital in 1890. He qualified in 1895, graduated M.B., B.S. two years later, and proceeded M.D. in 1898. He had taken the F.R.C.S. in 1897 and went on to the M.S. in 1901, the year before he was appointed assistant surgeon to the hospital. He had already held the usual house appointments at the Westminster, and he had been to Liverpool as house-surgeon to Thelwall Thomas, whose teaching and example he always admired. He came also to some extent under the influence of Robert Jones.

Evans served with Charles Stonham in the South African War in the Imperial Yeomanry Field Hospital and Bearer Company. He was taken prisoner at Roodevaal by Christian de Wet, but a little later was retaken by British troops under Lord Methuen. Purves-Stewart was with him in South Africa, and together they wrote a little book on the treatment of injuries of peripheral nerves. After his return from the Boer War he took one of the special commissions in the Territorial Army open to members of the staffs of teaching hospitals, and so he was mobilized at the outbreak of the 1914–18 war and attached to the 4th London General Hospital. He also had charge throughout the war of the hospital for officers at Alford House, Park Lane.

In 1929 Evans was a Hunterian Professor at the Royal College of Surgeons, and by this time he held many hospital appointments. He was on the staff of the Royal Masonic, the Royal Hospital for Diseases of the Chest, Bethlem, the Temperance Hospital, the Seamen's Hospital Society at their dock branch hospital, and he also helped one or two cottage hospitals. His surgical interests therefore were general, and his sound basic training enabled him to apply first principles in all fields and made him an excellent teacher. He was notably generous in his attitude to his registrars and took great pains with the training of his house-surgeons. His general manner and kindly bearing endeared him to all his patients. Following Stonham, he had always been interested in the surgery of the oral cavity, and when radium became available he devoted a lot of attention to the development of the technique of its application.

Evans was a man of strong character, with a delightful vein of humour running through it that made him a most attractive colleague. He used to say that he ought to have been on the music-hall stage; and indeed, with his fine tenor voice and acute sense of the comic, he certainly could have made a success. He used that capacity at times with remarkable effect; he could resolve the tension of a discussion tending to become acrimonious with one funny remark that had a kernel of obvious common sense. Common sense, good judgment, a warm heart, and high principles made him a good doctor as well as a first-class surgeon. He found his relaxation in music and golf. His long and very trying last illness was borne with great fortitude and courage. He was very happy in his family life and proud that two of his sons should be surgeons.

THOMAS H. MILROY, D.Sc., M.D., F.R.S.Ed.

Dr. T. H. Milroy, who was emeritus professor of physiology in Queen's University, Belfast, died suddenly at his home in North Berwick on March 20.

Thomas Hugh Milroy was born in 1869, the eldest son of the late John Milroy, of Kirkcowan, Wigtownshire. He was a student at the universities of Edinburgh, Berlin, and Marburg, and graduated M.B., C.M. in 1891, proceeding M.D. in 1896. He had taken the B.Sc. in public health in 1892 and he was later elected F.R.S.Ed. Dr. Milroy was for a time lecturer on physiological chemistry and senior assistant to the professor of physiology at Edinburgh University. From these early days he was greatly interested in the physiology of muscle contraction, a subject on which he contributed some valuable papers to the special journals. He and his brother, the late Dr. J. A. Milroy, were jointly responsible for the well-known *Textbook of Physiological Chemistry*, the third edition of which was published in 1921.

As professor of physiology at Queen's University, Belfast, Milroy continued his research work and over the years he received a number of honorary degrees. The D.Sc. of the National University of Ireland was conferred on him, the M.D. of Dublin University, and Belfast itself made him an honorary D.Sc. After his retirement from the chair at Belfast, Professor Milroy continued to undertake certain work in which he was particularly interested in the physiology department of Edinburgh University, where he was awarded an honorary LL.D. He was vice-president of the section of anatomy and physiology at the annual meetings of the B.M.A. in 1909 and in 1927, and he was president of the section of physiology and biochemistry in 1933. He was a man with a quiet and unobtrusive nature; yet he contributed a great deal to the development of his special branch of physiology, and he had always a charming personality which endeared him to his intimate friends.

Dr. GEORGE THELWALL K. MAURICE died on March 8 at his home in Marlborough, where he was born in March, 1867. He was the son of the late James B. Maurice, M.D., F.R.C.S., one of a family long known and highly respected in that part of Wiltshire. He was educated at Marlborough College and St. Mary's Hospital, where he qualified as M.R.C.S., L.R.C.P. in 1890. He decided not to join the family practice but to seek a career in the R.A.M.C. When the war of 1914–18 began he was a major, and at once went to France as second in command of a field ambulance in the Third Division, with which he took part in the retreat from Mons. Shortly after the beginning of the campaign Maurice was given command of another ambulance in the same Division. In those days there were no motor ambulances in the British Army—all ambulance transport was horse-drawn. Maurice was a keen lover of horses and field sports, and he revelled in the care of his teams, a job which many R.A.M.C. officers had for lack of expert knowledge to delegate to junior officers. He was later posted to Malta, where he and Field-Marshal Lord Methuen built up a hospital service which deserved and attracted widespread appreciation. Later he became a D.M.S. in Macedonia, and after the campaign in Peshawar he served in the Afghan War of 1919, for which he gained the medal. He was mentioned several times in dispatches, and made C.M.G. and C.B.E. He retired with the rank of colonel to his own homeland at Marlborough. He published a book of nature observations. George Maurice married Olive, daughter of the late Sir Henry C. Burdett, K.C.B., K.C.V.O.

Surgeon Captain ROBLEY BROWNE, R.N., O.B.E., who died on March 20, had a long and varied medical career. He was born in 1863, studied medicine at Guy's Hospital in the 'eighties, and qualified in 1887. He entered the Royal Navy as a surgeon, remained in the Service until after the first world war, and retired with the rank of surgeon captain. During his career he was privileged to serve in the Royal Yacht, and he had many happy recollections of the spacious days of King Edward VII and Queen Alexandra. One of his last posts, and one of which he was particularly proud, was that of P.M.O. in the *Lion*, under Admiral Beatty's command. After he retired from the

Navy he enrolled as a ship surgeon to the White Star Line, and crossed the Atlantic many times in the *Olympic* and other liners. He married relatively late in life. Soon after he retired from the sea his wife opened a boarding school for girls, a project in which he found a new sphere of service and interest.

Robley Browne possessed an exceptionally good memory, accurate both for names of persons and places. He disliked ambiguities and uncertainties and would take endless trouble to be sure of his facts. To the end of his life he preserved a youthful buoyancy of carriage, a quick and friendly eye, and a running flow of easy conversation. His friends knew that for more than fifty years he had kept a diary written each day in his bold clear handwriting. Within a few minutes he could refer to incidents which had occurred during the Boxer rebellion in China in the 'nineties, or to an experience when serving in the Royal Yacht, or to impressions of some celebrity encountered when serving in the White Star or Cunard Lines. Until a few weeks ago he continued to drive his own car and to fill up his time with missions of one sort and another undertaken on behalf of others. He had a knack in engaging in these in a characteristically unobtrusive and self-effacing way, as though doing these little services as a matter of course and without any expectation of acknowledgment.—C. D.

Medico-Legal

DAMAGES FOR BLOOD DONOR

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Mrs. Ivy Lowen, of Shoeburyness, gave blood eight times without ill effect at the Rochford Municipal Hospital. After the ninth occasion on which she acted as a blood donor her right arm became septic and as a result she has a long permanent scar. Suing the hospital and the medical officer, Dr. P. W. Hopper, who took the blood, she alleged that members of the staff had neglected to take proper antiseptic measures; and that she had reported to the sister immediately after the operation that she was losing an undue quantity of blood, but the sister had negligently failed to make a proper examination and to replace the sodden dressing.

At the trial of the action in the High Court before Mr. Justice Hilbery and a jury,[1] Dr. Hopper was dismissed from the case for lack of evidence of negligence, but the jury found that the hospital had been negligent. In his summing-up the judge said the fact that the arm became septic after the operation did not establish negligence on the part of the hospital, acting through either the surgeon or the nurses. There was no evidence of any failure to take proper antiseptic precautions, and evidence had been given that the instruments were properly sterilized. Even if the jury believed that there had been a want of reasonable skill and care, they would still have to ask themselves whether the proper inference was that that was the cause of the arm becoming septic. Expert evidence had been given that deep layers of the human skin could not be absolutely sterilized, and that even where the most thorough precautions were taken there was always a remote chance of infection being carried into a puncture.

After the jury had given their verdict in favour of the donor, counsel representing the Ministry of Health (which took over the hospital after the action was started) submitted that there was no evidence of lack of proper antiseptic measures or of any breach of duty by the nursing sister, and that the cause of the infection remained a matter of speculation, with the preponderance of opinion that it was carried in by the needle.

The judge ruled, however, that there was some evidence from which the jury might infer that the germs had entered the donor's system from the blood-soaked dressing. He awarded her £200 damages with costs, including the costs she would have to pay to Dr. Hopper.

[1] *Scotsman*, February 22, 1950.

Medical Notes in Parliament

In the House of Lords on March 22 Lord SHEPHERD introduced the Medical Bill, to amend the Medical Acts and for purposes connected therewith. The Bill was read a first time without debate, and its main provisions are summarized elsewhere in this issue (p. 782).

The Faculty of Homoeopathy Bill was read a second time in the House of Lords on March 21 and was referred to the examiners.

MIDWIVES BILL

Lord SHEPHERD in the House of Lords on March 21 moved the Second Reading of the Midwives (Amendment) Bill. He said a working party to consider the conditions under which midwives worked and were trained had reported on January 28. The report contained 63 tabulated recommendations, but only a small proportion of these had to be considered with reference to future legislation. By far the greater number had been put into operation, or, if they were accepted by the Government, would be put into operation administratively. He recalled that it was not until 1902 that the first measure had been placed on the Statute Book dealing with the employment of midwives, their education, training, and registration. Since then, and especially since the Act of 1936, this profession had become recognized, its members were well trained and certificated, and were now employed by public authorities.

At present 70,000 midwives had their names on the Roll, of whom some 18,000 were practising. Of this smaller number 5,800 were employed by hospital authorities and 8,200 by local authorities. He explained that the figures cited all related to England and Wales. He believed the Bill was acceptable in all quarters and would have an easy passage. The working party for nurses had recommended that the Central Midwives Board should be amalgamated with the General Nursing Council. Later, when a second working party was established for midwives, the Government asked it to express an opinion on this recommendation, and the second working party decided it would be much better if the control of midwives remained separate from that of nurses in general. The Government had decided to accept the latter view, and to that extent there would not be an amalgamation of the midwives service with that of nursing services in general.

Clauses 1 and 2 of the Bill dealt with the reconstruction of the Central Midwives Board and the Central Midwives Board for Scotland. Hitherto these boards had been appointed by Order in Council. The Government had now decided to ask Parliament to alter that method and to allow changes in these boards to be made by statutory instrument. That would retain the right of Parliament to intervene when changes in the boards came up for consideration. Any changes would not imply a reflection on the efficiency of the boards but would be designed to strengthen them by inclusion of a higher proportion of qualified midwives.

Clauses 3 and 4 of the Bill concerned the certification of midwives who had passed their examinations in one of the countries of the United Kingdom. A midwife certificated in England would become eligible for registration and certification in Scotland under rules made by the Scottish Central Midwives Board.

Clause 5 dealt with women who had been trained as midwives in other countries. Clause 6 concerned uniforms. An official uniform was to be provided, but its wearing

would not be compulsory. The penalty for wearing it without proper authority would be severe.

Clause 7 covered the Roll of Midwives. There were 70,000 enrolled, and the Central Midwives Board was compelled to publish this Roll every five years. It was considered a waste of time and money for the full Roll to be published. It would be kept at the headquarters of the Board, and a duty of the Central Midwives Board would be to publish each year a list of practising midwives. Clause 8 enabled the local supervising bodies to provide residential accommodation for pupil midwives, and Clause 9 exempted from jury service midwives who were in practice. Clause 10 would facilitate a consolidation measure so that the law relating to midwives could be made clear and simple.

Lord LLEWELLIN said there was no objection at all to the measure. He thought it a good idea that midwives should have a distinctive uniform, and hoped it would not be a kind of county council uniform adapted to anyone doing any kind of service in the county council. Exemption from jury service ought to have been provided a long time ago.

Lord WEBB-JOHNSON welcomed the Bill. He asked Lord Shepherd to consider before the committee stage the wording of Clause 6. He had been disturbed to find that some local authorities might prevent midwives from wearing the uniform of their profession.

Lord SHEPHERD promised to consider the point made by Lord Webb-Johnson. He also promised to provide statistics relating to midwives in Scotland.

The Bill was then read a second time and was committed to a full committee of the House.

Kingston Hospital

Mr. BOYD-CARPENTER raised on March 21 questions concerning appointments in the South-west Metropolitan Regional Hospital Board, and hoped the Minister would accept the view that an inquiry must take place. A dispute had arisen over appointments to the Kingston Group London Committee. Behind this dispute was another between the group management committee and the regional hospital board on whether the Kingston Victoria Hospital should continue as a small hospital to which general practitioners could go to treat their patients or whether it should be turned into a maternity unit attached to a larger hospital.

Renewal of appointments to the management committee had become due, and in the last few days the chairman of the management committee and three of the members had not been reappointed. All had strongly supported the views of the management committee against the views of the regional board. They had taken the view that the group management committee's views were more in accord with local needs and local tradition than were the recommendations of the regional board. It appeared to him that the regional board had used its powers of appointment to force its views upon the management committee. The Third Schedule of the Act of 1946 laid down that before making appointments to fill vacancies the board should consult the management committee. He understood that that consultation had not taken place. The chairman had been replaced by an admiral who came from outside the hospital area. This was part of an attempt, and he believed it was not the only attempt, which this particular regional board had made to exercise its powers of appointment to override the group management committee. The management committee's object was to secure that local feeling and local views were properly represented.

Mr. Boyd-Carpenter added that at the time of these appointments the local advisory committee was asked for recommendations for appointments to the group committee. The advisory committee had nominated four medical men in order of preference. The regional board appointed the two at the bottom of the order of preference. The doctor whose name appeared first in the order of preference was a man prominent in the activities of the British Medical Association, who shared the views of the group management committee on the future of the Victoria Hospital. There remained on the group management committee a man who was not only a member of the regional board but also in his medical capacity an employee of the group management committee. He asked Mr. Blenkinsop to give an assurance that the matter would be investigated and that the Minister would discuss it not merely with the regional board but with members and former members of the group management committee.

Mr. MCCORQUODALE supported Mr. Boyd-Carpenter and said that the former chairman of the Kingston Group Management Committee had long and successful experience of hospital administration.

Mr. MESSER hoped the Minister would not give in to the appeals which had been made to him. When the Act was passing through the House of Commons the Opposition had said the Minister of Health must not do anything to interfere with the responsibilities placed on the regional hospital board. The regional boards were independent and had the power of appointing management committees. The nominations made by the management committee had gone first to the South Surrey Area Committee, which had sent the recommendations to the area regional board. There had been consultation to the extent that the area committee was the agent of the regional board for this purpose. The members in question had terminated their appointment. The chairman had resigned and afterwards asked for the resignation to be withdrawn.

Mr. BLENKINSOP said that quite properly Mr. Bevan had no power to deal with the appointment of hospital management committees. The Ministry was satisfied that the regional hospital board had carried out its duties to the letter. Mr. Bevan had sent advice to regional hospital boards on the size of management committees, on the different bodies that should be consulted in addition to those laid down in the schedule, and on the desirability of change from time to time in the membership of hospital management committees. The desirability of getting new personnel on these committees was a matter which the Ministry also considered in the appointment of regional hospital boards. If, when it made changes in these boards, the Ministry was to be checked in the manner suggested it would be impossible to bring new blood to the board. Similarly, the Ministry desired to encourage the regional hospital boards in their turn to bring new personnel into the management committees. If the regional hospital boards were to be attacked when they desired to make changes in the membership of management committees, few members or chairmen of regional hospital boards would accept the heavy responsibilities imposed on them under the Act.

On March 23 Mr. BOYD-CARPENTER asked Mr. Bevan why the chairman and three members of Kingston Group Management Committee had not been reappointed and whether the decision not to reappoint these persons had been approved by him.

Mr. BEVAN said the making of these appointments was a duty placed by statute on the regional hospital boards, and no question of his approval arose.

On the same day Mr. BOYD-CARPENTER also asked Mr. Bevan whether it was with his approval that paid servants of regional hospital boards or group hospital management committees were appointed members of the boards or committees by whom they were employed.

Mr. BEVAN said that as a general principle he was not in favour of these officers serving as members of the bodies with which they were immediately connected. The requirements of the Acts made it inevitable, however, that a limited number of the senior medical and dental staffs should be so appointed, and he recognized that there might be other exceptional cases where it was desirable so to appoint officers.

Commander NOBLE asked if Mr. Bevan knew there was a widespread feeling that there were political backgrounds to these appointments.

Mr. BEVAN replied that this was a point he had not yet been able to establish, but many Labour M.P.s told him they were satisfied that, in some instances, Conservatives had been put on these committees.

Iodized Salt

Mr. SOMERVILLE HASTINGS on March 22 asked whether the Food Standards Committee had completed its inquiry into the measures necessary to give effect to the Medical Research Council's recommendation that all domestic salt supplies in Great Britain should be iodized as a measure of protection against goitre.

Mr. MAURICE WEBB replied that this had been done, and presented briefly to the House the recommendations of the Food Standards Committee. These recommendations and the considerations which prompted them are presented fully elsewhere in this issue (p. 783).

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

The Rockefeller Foundation has provided a sum of up to £5,000 to the University for research in neurophysiology under the direction of Professor E. D. Adrian, O.M., F.R.S., during the five-year period beginning February 1, 1951, not more than £1,500 to be available in any one year.

The following have been appointed Associate Lecturers in the Faculty of Medicine for three years from January 1 in the subjects indicated: *Physic*, L. B. Cole, M.D., F.R.C.P., L. C. Martin, M.D., F.R.C.P., and A. P. Dick, M.D., M.R.C.P. *Surgery*, P. H. R. Ghey, M.Chir., F.R.C.S., V. C. Pennell, M.B., B.Chir., F.R.C.S., and B. McN. Truscott, M.B., B.S., F.R.C.S. *Orthopaedic Surgery*, R. W. Butler, M.D., M.Chir., F.R.C.S., and T. J. Fairbank, M.B., B.Chir., F.R.C.S. *Otolaryngology*, A. S. H. Walford, M.B., B.Chir., F.R.C.S., and K. F. Wilsdon, B.M., B.Ch., F.R.C.S.Ed. *Ophthalmology*, B. G. Recordon, M.D., and G. F. Wright, M.B., B.Chir., D.O.M.S. *Thoracic Surgery*, G. Kent Harrison, M.D., F.R.C.S. *Obstetrics and Gynaecology*, O. Lloyd, M.D., F.R.C.S., M.R.C.O.G., and Janet E. Bottomley, M.D., F.R.C.S., M.R.C.O.G. *Paediatrics*, D. M. T. Gairdner, D.M., M.R.C.P. *Dermatology*, C. H. Whittle, M.D., F.R.C.P. *Psychiatry*, E. B. Davies, M.D., D.P.M., and R. A. Noble, M.B., Ch.M., M.R.C.P., D.P.M. *Radiology*, Ff. Roberts, M.D., D.M.R.E., F.F.R., and F. R. Berridge, M.B., B.Chir., D.M.R.

UNIVERSITY OF EDINBURGH

Dr. Douglas Guthrie, Lecturer on the History of Medicine in the University, will deliver a series of lectures entitled "A Retrospect of Medicine and Science" on April 18 and 24, May 1, 8, 24, and 29, and June 5, 12, and 19. On May 15 Dr. J. Menzies Campbell will present "A Survey of British Dentistry, 1685 to 1921"; and on June 22 Professor R. Shryock (Johns Hopkins University, Baltimore, U.S.A.) will discuss "Social Medicine in the Nineteenth Century." All the lectures will be delivered in the Physiology Lecture Theatre, University New Buildings, Teviot Place, Edinburgh, at 5 p.m. The course is open to all matriculated students and graduates of the University and to members of the University staff without fee. Others may attend on payment of an entrance fee of 10s. in lieu of the matriculation fee. Details of the lectures will appear in the "Societies and Lectures" column of the *Journal* week by week.

UNIVERSITY OF WALES

WELSH NATIONAL SCHOOL OF MEDICINE

The Council of the Welsh National School of Medicine has appointed Arthur Goronwy Watkins, M.D., F.R.C.P., to the newly established Professorship of Child Health at the Welsh National School of Medicine. Dr. Watkins has been Lecturer in Paediatrics since 1932 and is at present paediatrician to several hospitals and to the Tuberculosis Service in South Wales, and Adviser in Paediatrics to the Welsh Regional Hospital Board.

UNIVERSITY OF MANCHESTER

On Founder's Day, May 17, the honorary degree of D.Sc. will be conferred on Victor Ewings Negus, M.S., F.R.C.S., Surgeon to the Ear, Nose, and Throat Department, King's College Hospital, for his contributions to medical research, particularly in laryngology, and on the Right Honourable Lord Boyd-Orr, D.S.O., *M.C.*, J.P., M.D., D.Sc., LL.D., F.R.S., formerly Director-General, United Nations Food and Agricultural Organization, for public services and contributions to agricultural research.

No. 10

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended March 11.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1950					1949 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Meningococcal infection	27	1	18	2	2	33	2	13	—	1
Deaths		1	—				—	1		
Diphtheria	62	8	19	2	1	101	13	28	2	5
Deaths	—	—	—	—	—	—	—	1	—	1
Dysentery	362	11	90	2	—	65	5	23	—	2
Deaths					—					—
Encephalitis, acute	4	—	—	—	—	2	1	—	1	1
Deaths		—					—			
Erysipelas			22	10	10			33	8	4
Deaths										
Infective enteritis or diarrhoea under 2 years				13					49	
Deaths	18		3	2	—	28		—	4	—
Measles*	5,476	60	195	68	439	18,619	1081	166	175	214
Deaths†			—	1	—			—	—	—
Ophthalmia neonatorum	34	3	13		—	34	—	9	—	—
Deaths										
Paratyphoid fever	8	—	1 (B)		—	5	—	3 (B)	—	—
Deaths	—		—		—	—		—		—
Pneumonia, influenzal	1,014	60	26	—	26	1,500	72	33	11	21
Deaths (from influenza)‡	108	14	14	—	2	259	48	11	1	5
Pneumonia, primary			292	¶				261	51	
Deaths	355	68		10	16	458	75		11	17
Poliomyelitis, acute	41	3	4	6	—	10	—	2	—	—
Deaths§	2	1		—		1	—			
Puerperal fever		—	7				—	7		
Deaths										
Puerperal pyrexia‖	106	11	3		—	103	6	9	1	—
Deaths										
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	2,093	123	176	77	127	1,189	54	182	101	30
Deaths†			—	—	—			—	—	—
Smallpox	—	—	—		—	—	—	—	—	—
Deaths					—				—	—
Typhoid fever	4	1	1	3	1	4	—	—	3	—
Deaths	—	—	—		—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths					—				—	—
Whooping-cough*	1,917	77	361	73	53	2,653	218	247	106	66
Deaths	3	1	—	—	1	7	—	1	—	—
Deaths (0–1 year)	301	37	48	15	12	318	40	44	15	11
Deaths (excluding stillbirths)	6,081	937	722	195	151	6,502	1010	717	181	176
Annual death rate (per 1,000 persons living)			14·5					12·7	10·9	
Live births	7,837	1274	946	399	222	7,438	1215	929	357	259
Annual rate per 1,000 persons living			19·0					18·6	22·1	
Stillbirths	216	27	28			178	35	29		
Rate per 1,000 total births (including stillborn)			29					30		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

EPIDEMIOLOGICAL NOTES

Smallpox

A nurse in a Glasgow hospital was taken ill on March 23, developed a rash two days later, and has now been diagnosed as a case of confluent smallpox. There are now two other confirmed cases in the same hospital, but in both the attack has been modified by previous vaccination. In a fourth case the disease is likely to run a mild course, and yet another patient and a baby are under surveillance. The source is probably a Goanese seaman who landed from the R.M.S. *Chitral* at Tilbury on March 5 and travelled to Glasgow. He was taken ill on March 7, and developed a rash soon after admission to hospital on March 10. Chickenpox was diagnosed. This man was probably infected on the *Chitral*, and there may be another missed case or cases among the passengers and crew disembarked in London on March 5. Smallpox should be suspected in any passenger or contact who reports sick with fever or a rash.

Discussion of Table

In *England and Wales* infectious diseases were more prevalent during the week and there were increases in the notifications of measles 792, scarlet fever 335, whooping-cough 303, and dysentery 82.

The largest rises in the notifications of measles were Durham 157, Staffordshire 131, Yorkshire West Riding 97, Lancashire 94, Glamorganshire 82, Suffolk 65. An increase in the incidence of scarlet fever occurred in every region of the country; the largest of the local rises were Lancashire 57 and Yorkshire West Riding 31. A small increase in whooping-cough occurred throughout the country, but the only local rise of any size was Yorkshire West Riding 77. The chief feature of the returns of diphtheria was a decrease of 8 in London.

The largest notifications of dysentery were Yorkshire West Riding 128 (Sheffield C.B. 62, Bradford C.B. 23, Leeds C.B. 23, Dewsbury C.B. 8); Durham 79 (Blaydon U.D. 36, Stanley U.D. 15, South Shields C.B. 13); Lancashire 44 (Manchester C.B. 34); Northumberland 36 (Newcastle-upon-Tyne C.B. 30); Glamorganshire 14 (Cardiff C.B. 13); Nottinghamshire 13 (Nottingham C.B. 13); Cheshire 10 (Birkenhead C.B. 9); and Gloucestershire 10 (Bristol C.B. 10).

In *Scotland* there were increases in the notifications of whooping-cough 58, measles 49, acute primary pneumonia 62, and dysentery 22. The rise in dysentery was contributed by Glasgow, where the notifications rose from 22 to 42. The other large returns of dysentery were Edinburgh 18 and Dundee 16. The rise in the incidence of measles and acute primary pneumonia was attributed to Glasgow.

In *Eire* a decrease of 26 in the notifications of measles was the only variation of any size in the totals of infectious diseases.

In *Northern Ireland* an increase of 23 notifications of measles and a decrease of 19 notifications of scarlet fever were recorded. The only fluctuation of any size in the local trends was a rise in the notifications of measles in Antrim county of 27.

Week Ending March 18

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,837, whooping-cough 2,231, diphtheria 62, measles 5,577, acute pneumonia 1,078, acute poliomyelitis 27, dysentery 398, paratyphoid fever 3, typhoid fever 5. In the great towns 167 deaths were attributed to influenza.

Hospital authorities are asked by the Ministry of Health to consider the desirability of establishing assistant-nurse training schools in as many of their hospitals as possible that are suitable for the purpose. A Ministry circular says that the hospital service employs full-time some 17,000 people classified as nursing staff with no statutory or other recognized qualification. Many of these would be quite capable of taking the revised course of training for the Assistant Nurses Roll if facilities were available.

Medical News

Antihistamines and the Common Cold

In view of the conflicting reports on the value of antihistamine drugs in the treatment of the common cold, the Medical Research Council has agreed to arrange an investigation. Trials are being carried out in factories, Civil Service establishments, and other institutions where large numbers of subjects can be studied. Volunteers are requested to report when they have a cold, and they are then given tablets to take and the progress of the cold is assessed during the next week. Some of the volunteers are given tablets containing the antihistamine drug under trial; others get tablets containing another compound. In order to obtain results which are scientifically sound, neither the volunteer nor the doctor conducting the test is aware of which type of treatment is being given. It will necessarily be several months before the results of the tests are known.

Surgery Prizes

The Association of Surgeons of Great Britain and Ireland has decided to award annually in place of the Moynihan Fellowship a Moynihan Prize of £100, together with a medal, for an essay. The subject for 1951 will be "Pathology, Prevention, and Treatment of Thrombophlebitis (Including Phlebothrombosis)," and for 1952 "Pathology of the Formation of Calculi." Essays and dissertations for the 1951 prize must be received by the honorary secretary of the association not later than March 31, 1951, and for the 1952 prize not later than December 31, 1951. Further details can be obtained from the honorary secretary at 45, Lincoln's Inn Fields, London, W.C.2.

Fellowships in Medicine and Tuberculosis

The Medical Research Council invites applications for the following Fellowships: the Rockefeller Medical Fellowship, intended for graduates resident in the U.K. who have had some training in research in clinical medicine or surgery or medical science, and who are likely to profit from working at a centre in the U.S.A. or elsewhere abroad before taking up positions for higher teaching or research in the U.K. ($2,600 a year for a single Fellow or $3,600 a year for a married Fellow, plus travelling and other allowances.) Dorothy Temple Cross Research Fellowships in tuberculosis for study elsewhere in the U.K., ordinarily for one academic year, for suitably qualified British subjects intending to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis in all or any of its forms (£650 a year for a single Fellow, or £900 a year for a married Fellow, plus allowances). Further particulars and forms of application may be obtained from the secretary, Medical Research Council, 38, Old Queen Street, Westminster, S.W.1, with whom applications must be lodged before June 1.

National Formulary Amendments

The Joint Formulary Committee has made certain amendments to the *National Formulary*. They are entitled the First Amendment (1950). Notices prepared by the Ministry will be sent to doctors, chemists, and dentists. The amendments include the following: (*a*) Compound tablets of colocynth and jalap will be sugar-coated. (*b*) Conspersus talci boricus, *B.P.C.*, which appears in the General Section of the *National Formulary*, has now been added to the Infants Section. (*c*) Purified talc, sterilized: when talc is an ingredient of the dusting powders given in the *National Formulary*, purified talc, sterilized, must be used.

Deputy Lieutenant

Colonel John Livingston Hamilton, *M.C.*, T.D., of Creffield House, 2a, Oxford Road, Colchester, has been appointed Deputy Lieutenant in the County of Essex.

Hunterian Prize Essay

The Hunterian Prize Essay for 1949 has been won by Dr. S. M. Rivlin for his essay on the "Treatment of Varicose Veins and their Complications." The subject for the 1950 essay is "The Diagnosis and Treatment of Irritating Rashes." The competition is open to all general practitioners. Further details may be had from the honorary secretary, Mr. Clement Francis, 75, Wimpole Street, London, W.1.

Institute of Social Psychiatry

The institute is appealing for £25,000 to encourage research, to develop the institute's social rehabilitation scheme for offenders, and to open new therapeutic social clubs. At a dinner held on March 22, which was presided over by Colonel J. J. Astor, Dr. E. B. Strauss emphasized the need for further funds to carry on the institute's work for mental health and public welfare. Sir John Charles, Deputy Chief Medical Officer of the Ministry of Health, referred to some of the problems of a national medical service, asking, Was ear piercing a surgical procedure, and was slimming of the female form medical or cosmetic treatment? The institute's activities had been most beneficial, and great opportunities lay ahead. Alderman Reginald Stamp, chairman of the Health Committee of the L.C.C., said that the L.C.C. contributed only 90% towards the institute's expenses because it believed in voluntary service, leaving the other 10% to be raised voluntarily. Dr. Noel Harris recalled the past, when patients were sometimes brought to hospital in strait-jackets. The attitude of the public had done much to put patients off mental treatment, but that was changing. There was a great shortage of trained psychiatrists. The institute was hoping to contribute to the study of delinquency. Colonel Astor gave the toast of "The Institute," which was replied to by Dr. J. Bierer.

Wills

Dr. William Lyle, who was Unionist M.P. for Queen's University in the Northern Ireland Parliament, left £22,542. Dr. Richard Walter Marsden, formerly medical superintendent of Crumpsall Hospital, Manchester, left £27,674; Dr. William Cunningham Milroy, of Wallasey, £56,285; Dr. Francis Griffith Thomas, formerly ophthalmic surgeon to the Swansea General and Eye Hospital, £18,724; Dr. Richard Picton Rosser, of Darlington, Durham, £20,850; and Dr. Henry Corsi, of Harley Street, W.1, £29,731.

COMING EVENTS

Medical Art Society

The annual exhibition of the Medical Art Society will take place at Walker's Galleries, New Bond Street, London, W., from April 17 to 29. The annual dinner of the Society will be held at Kettner's Restaurant, Romilly Street, London, W., on Monday, April 17, at 7 p.m.

British Medical Students Association

The following meeting has been arranged. *Northern Region.*—April 4: Regional meeting at Leeds.

Royal Eye Hospital

The Royal Eye Hospital (King's College Hospital Group), St. George's Circus, London, S.E., has arranged a series of spring-term lectures open to postgraduate and undergraduate students. A fee of £5 5s. per subject will be charged for physiology and anatomy and for the practical courses on pathology and bacteriology, refraction, and operative surgery. Those wishing to attend any of the lectures, or the classes, are requested to apply for tickets of admission. The lectures on clinical ophthalmology and the occasional lectures are free of charge.

Rehabilitation Conference in Argentina

A conference on rehabilitation will be held at Buenos Aires in October, 1950. Particulars may be obtained from the Secretary, Organizadas por el Ateneo de Kinesiologia, Facultad de Ciencias Medicas, Buenos Aires.

SOCIETIES AND LECTURES

Monday

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W., April 3, 8.30 p.m., "*Ulcerative Colitis*," discussion to be introduced by Professor T. L. Hardy and Mr. Michael J. Smyth.

Tuesday

CHADWICK PUBLIC LECTURE.—At London Missionary Society, 42, Broadway, Westminster, S.W., April 4, 2.30 p.m., "*Rivers Pollution and the River Boards Act, 1948*," by Mr. C. E. Scholefield.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., April 4, 5 p.m., "*Congenital Defects of Testicle and Epididymis*," by Mr. H. Rees.

ROYAL EYE HOSPITAL (KING'S COLLEGE HOSPITAL GROUP), St. George's Circus, London, S.E.—April 4, 5 p.m., "*Science and Art of Refraction*," by Dr. T. H. Whittington.

Wednesday

INSTITUTE OF UROLOGY.—(1) At St. Peter's Hospital, Henrietta Street, Covent Garden, London, W.C., April 5, 3.30 p.m., *X* rays and Museum Specimens, by Mr. H. K. Vernon; (2) At St. Paul's Hospital, Endell Street, London, W.C., April 5, 5 p.m., "*New Growths of the Bladder*," by Mr. J. G. Sandrey.

NATIONAL HOSPITAL, Queen Square, London, W.C.—April 5, 5 p.m., "*Neurofibromatosis of Central Nervous System*," by Professor J. Morelle (Louvain).

Thursday

ROYAL EYE HOSPITAL (KING'S COLLEGE HOSPITAL GROUP), St. George's Circus, London, S.E.—April 6, 5 p.m., "*Affections of the Fundus*," by Mr. Arnold Sorsby.

APPOINTMENTS

Dr. Norman George Bisset McLetchie has been appointed to the chair of pathology at Dalhousie University, Halifax, Nova Scotia, in succession to Professor R. P. Smith.

Dr. McLetchie qualified at Glasgow in 1938, and proceeded M.D. with honours in 1944. He was Director of Pathological Laboratories at Regina, Saskatchewan before his present appointment.

ASTLEY, CLIFFORD E., M.D., M.R.C.P., Consulting Physician, Tees-side Group of Hospitals.

BURNS, J. P. J., *M.C.*, M.B., B.Ch., D.P.H., Deputy Medical Officer of Health, County Borough of Great Yarmouth.

CHARRETT, MACDONALD ARTHUR, M.R.C.S., L.R.C.P., D.P.H., Medical Officer of Health to the Borough of Slough and Area Medical Officer for South Bucks.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Consultant Paediatrician in the Peterborough Area*, G. H. Valentine, M.B., Ch.B., M.R.C.S., M.R.C.P.

FOULKES, SIEGMUND H., M.D., L.R.C.P.&S.Ed., Part-time Physician (Consultant), Bethlem Royal Hospital and the Maudsley Hospital, Denmark Hill, London, S.E.

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Whole-time Consultant Anaesthetist to hospitals in North Liverpool and adjoining areas*, J. Davidson, M.B., Ch.B., D.A.; *Part-time Consultant Anaesthetists to hospitals in North Liverpool and adjoining areas*, S. Lipton, M.B., Ch.B., D.A., and P. B. Conroy, M.R.C.S., L.R.C.P., D.A.; *Consultant Resident Deputy Medical Superintendent to Rainhill Hospital*, G. P. Egan, M.D., D.P.M.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Fawkes.—On March 3, 1950, at Port-of-Spain, Trinidad, to Hilary (née Holton), wife of Dr. M. A. Fawkes, a son—Richard de Fontenelle.

Giles.—On March 14, 1950, to Ruth (née Whitley), wife of Dr. Christopher Giles, Wayside, Sandy Lane, Newcastle, Staffs, a son.

McCracken.—On March 15, 1950, at Hope Hospital, Salford, to Margaret (née Laycock) and Dermot McCracken, a son—Robert Henry Joy.

Schofield.—On March 18, 1950, at the Liverpool Maternity Hospital, to Marjorie (née Reeve), M.B., Ch.B., wife of Theo L. Schofield, F.R.C.S., a daughter.

DEATHS

Bellerby.—On March 21, 1950, Owen Henry Bellerby, M.R.C.S., L.R.C.P., of 35, Wear Bay Road, Folkestone.

Browne.—On March 20, 1950, at Hampden House, Great Missenden, Bucks, Robley Henry John Browne, O.B.E., M.R.C.S., L.R.C.P., Surgeon Captain, R.N., retired, aged 86.

Dunsmuir.—On March 14, 1950, at Hobart, Tasmania, Allan Dunsmuir, M.B., Ch.B., aged 67.

Dykes.—On March 18, 1950, at 54, London Road, Cirencester, Glos, Charles Reginald Dykes, M.R.C.S., L.R.C.P., formerly of Buckhurst Hill, Essex.

Evans.—On March 20, 1950, at Forest Green, Surrey, Arthur Henry Evans, O.B.E., M.D., M.S., F.R.C.S., aged 78.

Milroy.—On March 20, 1950, at Woodville, North Berwick, Thomas Hugh Milroy, M.D., D.Sc., LL.D., F.R.S.Ed.

Mitchell.—On March 19, 1950, Ada Mitchell, daughter of the late Dr. C. C. Greig, of Fyvie, and wife of Alexander Mitchell, Ch.M., of The Lodge, Old Rayne, Aberdeenshire.

Proctor.—On March 23, 1950, at 4, Tynedale Villas, Hexham, Northumberland, Alfred Henry Proctor, D.S.O., M.D., M.S., F.R.C.S.Ed., Colonel, I.M.S., retired.

Suffern.—On March 21, 1950, at Hill Head, Fareham, Hants, Alexander Canning Suffern, O.B.E., M.D., Lieutenant-Colonel, R.A.M.C., retired.

Twort.—On March 20, 1950, at his home in Camberley, Surrey, Frederick William Twort, M.R.C.S., L.R.C.P., F.R.S., aged 72.

Wilson.—On March 23, 1950, at Braeside, Wyche Road, Malvern, Worcs, Thomas Wilson, M.D., Ch.M., F.R.C.S.

Wolferstan.—On March 17, 1950, at Ashford County Hospital, Kenneth Wolferstan, M.R.C.S., L.R.C.P., of Sunbury-on-Thames, Middlesex, aged 65.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Viability of Common Bacteria

Q.—*(1) How long do the organisms responsible for an ordinary cold remain virulent and infectious in used handkerchiefs kept in a dirty-clothes basket? (2) How long do the ordinary streptococci, staphylococci, and bacilli remain infectious and virulent (a) if exposed to air and sunshine, and (b) if in damp and dark conditions?*

A.—There is no very reliable published evidence about the viability of the common cold virus in dried secretions outside the body. The stories of Antarctic explorers developing colds when stored clothing or blankets were brought into use should be accepted with some reservation, since it is impossible to say whether these "episodes" were caused by infectious coryza or some allergic reaction to dust and the like. The virus of influenza has been shown to remain viable for some weeks after natural drying, but in greatly reduced proportions.

Staphylococci, haemolytic streptococci, and diphtheria and tubercle bacilli will remain viable in dust for some weeks in the dark, but exposure to daylight, even through glass, has a fairly rapid lethal action, as Garrod and others have shown. During the process of natural drying the numbers of bacteria are very considerably reduced, and if dosage is important in initiating clinical infection the environment would probably have to be heavily contaminated, as may happen with a streptococcal *nasal* carrier, before it can serve as a means of transfer of infection. There is no evidence that the virulence of the organism is reduced by desiccation, but it seems likely that bacteria in the dried resting stage would be at a disadvantage against the host tissues, compared with actively multiplying organisms.

Acute Dilatation of the Stomach in Poliomyelitis

Q.—*Is acute dilatation of the stomach a common complication of acute paralytic poliomyelitis? For a patient in an iron lung, what treatment is advised and is there any possible prophylaxis?*

A.—This is a not infrequent complication of respirator therapy. However severe the paralysis, the writer has never encountered it in patients with poliomyelitis who were not in respirators, nor in children. The general atony of the gastro-intestinal tract connected with autonomic involvement and combined with lack of effective abdominal musculature may possibly provide a favourable set of circumstances for initiating the condition. Aerophagy may perhaps be a contributory factor, and also injudicious feeding (overloading). The abdominal wall elevation provided by the cabinet-type respirator may contribute by causing a negative intra-abdominal pressure. One should keep in mind the possibility of air being forced into the oesophagus when the patient is having assisted positive pressure lung inflation with machines of the resuscitator or lung-inflator pattern. In treatment, all gastric intake should be temporarily discontinued, and a Ryle's tube should be passed trans-nasally and retained. Through this drainage may be assisted intermittently or continuously by suction apparatus. Hydration may be maintained per rectum or intravenously. Prostigmin 0.5 mg. by injection thrice daily is often helpful, or carbachol 0.5 to 1 ml. intramuscularly, which may be repeated in a few hours.

Ejaculatio Praecox

Q.—*What is the best treatment for ejaculatio praecox? Are injections of male hormone of any value?*

A.—Ejaculatio praecox is not only the commonest but perhaps the most difficult form of sexual weakness to treat. For many years it was treated by physical measures alone; instillations of silver nitrate into the posterior urethra, cauterization of the verumontanum, the passage of instruments, prostatic massage, etc., but all with very poor results. It is now regarded as being generally an anxiety symptom, or an indication of a faulty attitude to sexuality. It is to be noted that a man who suffers from premature ejaculation may suffer from it when with one woman, but not when with another. It may also vary greatly on different occasions, according to the patient's state of mind. If a newly married couple can manage not to be too disturbed by it, it is likely to improve later. Small doses of bromide, or even a little alcohol, before intercourse may help some patients. So also does desensitizing the glans penis by the use of a 1% cocaine ointment. Hormone injections are not likely to have any effect. Cases in which there is no response to such simple measures should be referred to a psychologist.

On the psychological side ejaculatio praecox is commonly, but usually erroneously, regarded as due to a too great "keenness" or excessive desire on the part of the male. In many patients the opposite is the case, the premature ejaculation being a form of psychological inhibition akin to impotence. Some men on account of such inhibitions become completely impotent; others cannot altogether withhold the sexual urge, but avoid intercourse and achieve the same end by having a premature ejaculation. It should be emphasized that in both cases the inhibition is an unconscious one, and the man in question consciously has a desire to effect intercourse, but there is the unconscious resistance to it, usually due to some old fear. The so-called "keenness" is really a state of anxiety. That is why a man may be normally potent with one person, often a person free from sexual inhibitions, but will suffer from impotence or ejaculatio praecox with another person who for some reason or other arouses this inhibition. The approach to such a problem is to try to discover the causes of such fear and inhibition about sex, either from threats, circumcision, wrong teaching, an early sense of guilt, etc. If the patient can be brought to recognize such early taboos and their influence on the present day, he may be able to throw them off. Where the causes lie deeper expert analytic treatment is necessary. The trouble is that after several failures a vicious circle is set up, and the knowledge of past failures has a bad influence on further attempts. With newly married people, the best advice is not to worry about it, as it is a common experience which in most cases rights itself. The questioner should also consult the two articles on impotence which appeared in the *Journal* of March 25.

Residual Insecticides

Q.—*Water-miscible residual insecticides being the great answer to insect-borne house infections—malaria, filaria, and others—can details be given of a method of incorporating benzene hexachloride in distemper, with any references to the results of its use?*

A.—Benzene hexachloride and also D.D.T. can be incorporated in lime wash or distemper in various ways. The mixture remains toxic to insects, as shown by Hadjinikolau and Busvine (*Bull. ent. Res.*, 1948, **39**, 179). Water-miscible residual insecticides have recently been shown to be very efficient for treating absorbent surfaces such as plaster walls, because most of the insecticide remains on the surface and is therefore available to mak contact with the insect, instead of being absorbed into the wall. However, when such insecticides are mixed with whitewash or distemper much of the insecticide is covered up by particles of colouring matter; in fact, the latter acts as a diluent. Therefore there seems no virtue at all in mixing insecticides with a distemper. The best method is to apply a wash of insecticide to the surface of the finished wall.

Preparation for Dental Extractions

Q.—*What is the best way to tackle dental extractions in a patient who has bled considerably after previous extractions?*

A.—Severe recurrent haemorrhage following dental extraction may necessitate prophylactic and/or post-operative transfusions if it is shown that there is any abnormality in the clotting mechanism. The majority of cases, however, yield successfully to local treatment. It is important that the extraction should

be carried out with the minimum of trauma, and where there is a history of bleeding on previous occasions it is often advisable to apply pressure immediately the extraction has been completed. This can be done with sterile gauze or a cotton-wool roll held in position by closing the jaws tightly together. The various proprietary preparations containing extract of platelets, fibrinogen, etc., may be used on the gauze as an adjuvant. It is important that no plugging should be done into the socket itself, as stopping the normal formation of the blood clot results in bare bone being left, with inevitable sepsis and probably secondary haemorrhage. Light plugging over the top of the socket with "oxycel" may be of value in some cases. Lacerations of the gum are, of course, best treated by suture.

Dicoumarol in Thrombophlebitis

Q.—*Has any work been done on dicoumarol in thrombophlebitis migrans in this country? Granted that dicoumarol is a dangerous drug which can be given only under conditions of the most careful laboratory control, has the drug to be given for ever, like insulin, or are there any reports of cures? Is there any evidence that it removes the pain and disability from limbs chronically affected by previous attacks?*

A.—The results of the treatment of recurrent idiopathic thrombophlebitis are difficult to assess, because periods of quiescence often occur during the long episodic natural history of the disease. Anticoagulants have been used in this country for treating the acute phases of phlebitis. Pain and discomfort are relieved by such treatment. However, the long-continued use of either heparin or dicoumarol is impracticable, and recurrence of the disease is always possible when the administration of anticoagulants is discontinued. There is no evidence that the symptoms of chronic venous insufficiency are relieved by anticoagulants.

Toxic Effects of Vitamin D

Q.—*In the answer to a question about treating chilblains with vitamin D_2 (December 17, 1949, p. 1426) it was stated that toxic symptoms may appear with a dose of 100,000 units of vitamin D_2 daily. I took this dose for three weeks when suffering from cracked nails, and I felt well for the first time for about seven years. Can you tell me how long this dosage may be taken with safety, or how soon a short course may be repeated?*

A.—A feeling of well-being and a good appetite are often the first symptoms of vitamin-D poisoning. The dose that produces toxic effects varies with the individual. Toxic symptoms have been reported with doses of no more than 25,000 i.u. daily, while some patients have tolerated 200,000 to 400,000 i.u. daily. Toxic effects have also been reported after taking doses of the order of 500,000 i.u. daily for ten days. The best advice that can be given is this: avoid high doses of vitamin D for conditions that can be satisfactorily treated with other and safer therapeutic agents. The only conditions in which continued high dosage can be justified are lupus and resistant cases of rickets, and then careful biochemical and radiological control is necessary to avoid the dangers of overdosage.

Urticaria Pigmentosa

Q.—*Is there any effective treatment for urticaria pigmentosa? What is the aetiology of this condition, and what is the prognosis? The case I have in mind is a boy of 4 years, now severely disfigured; the condition began at the age of 5 months, appearing at first like a nettle rash.*

A.—The cause of urticaria pigmentosa is unknown. It probably indicates some congenital abnormality, either as regards metabolism or local mast cell response. The mast cells in the skin characteristic of this affection are packed with granules containing heparin, and in the very young this may occasionally be associated with some enlargement of liver. There is no treatment for the condition. When arising in children it disappears before they reach puberty, sometimes by the age of 6 or 7.

When the condition arises after puberty or in adult life it is usually persistent. If there is much trouble from associated urticaria and irritation the antihistamines may be used to control this.

Delayed-action Hypnotic

Q.—*Is there a "delayed-action" hypnotic suitable for occasional use by a somewhat highly strung patient who has little difficulty in falling asleep but is apt to wake early (4 or 5 a.m.) and has little hope of sleeping thereafter?*

A.—Sodium barbitone, which is a fairly long-acting barbiturate, in a dose of 5 or 7½ gr. would seem to be the most suitable drug to use in a case of this kind.

NOTES AND COMMENTS

Holidays Abroad.—Dr. H. B. M. MURPHY (Naples) writes: Your answer to the question under this heading ("Any Questions?" February 11, p. 385) takes a remarkably gloomy and old-fashioned view of holidays in Italy. While typhoid is still quite common here, and T.A.B. is advisable, malaria has almost disappeared from the country thanks to the Allied D.D.T. programme—and I do not think that either D.D.T. or proguanil should be bothered with. Culex is a little bit of a nuisance, and flies a great one, but D.D.T. will affect neither to-day and gammexane should be carried for them. Water can be considered safe if it comes from a main aqueduct, but water from wells is always suspect and surface water should never be used. It would be a shame if the advice about fruit was taken to be a warning against all except oranges or apples; washing of the fruit is important, but even more so is the danger of overeating, especially in country districts and of grapes. In towns and in the places a party of Scouts are likely to visit precautions are pointless. Every northerner of my acquaintance who has come to the south of Italy has undergone an attack of diarrhoea, but this has applied equally to people staying in the best of hotels and taking all precautions, such as the drinking of bottled water and eating no fruit. Better get through with it and forget it.

Amphetamine and Benedict's Solution.—Dr. FRANK MARSH (Epping, Essex) writes: The history of a patient I saw recently has some relevance to the answer given under this heading in "Any Questions?" (February 25, p. 502). Some days ago a healthy man of 30 was turned down by a Services medical board because his urine contained reducing substances. At the time of the medical examination he was suffering from a bad cold and had taken unstated quantities of aspirin together with 300 mg. of "anthisan" every day for three days before the medical board. The patient's enlightened general practitioner referred the patient to me for a glucose tolerance test. The patient reacted quite normally to 50 g. of glucose, and at no time had reducing substances in his urine. His urine was tested by his general practitioner the day after the medical board (when he had stopped taking drugs) with negative results. No doubt the explanation of your expert that amphetamine is a sympathomimetic drug and can raise blood sugar is also applicable to anthisan, and probably to most of these antihistamine remedies which are now so popular for the treatment of colds.

Teething Troubles.—Dr. N. R. CARLSON (Pevensey Bay, Sussex) writes: In reply to the question on teething troubles ("Any Questions?" March 11, p. 619) your expert advises the use of chloral hydrate. Quite by accident I discovered that "benadryl," either as the elixir or (in toddlers) as the 25-mg. capsules, given to the child at bedtime acts like a charm. Very few mothers have come back for more chloral, whereas they frequently return to me with glowing reports of peaceful nights and wanting a further supply of the "pink medicine." It is only benadryl that has this effect; the other antihistamine drugs do not produce such good results.

Jelly-fish and Weever-fish.—Lieutenant-Colonel F. W. W. DAWSON (Whangarei, New Zealand) writes: Dr. H. S. Russell (November 19, 1949, p. 1190) recommends for jelly-fish stings "anthisan" cream. Our beach is twenty miles from a chemist. I find that liq. iodi mitis, one application, also gives permanent and instant relief.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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